PROCEEDINGS

OF THE

NEW YORK PATHOLOGICAL

SOCIETY

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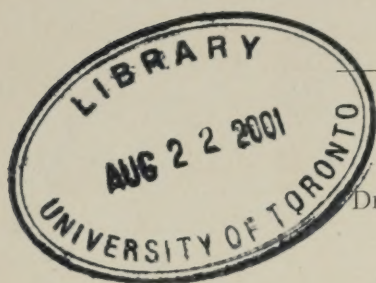
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New York Pathological Society.

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DR. HORST OERTEL, *President.*

OBSERVATIONS ON THE AUER BODIES IN ACUTE
LEUKEMIA.

REUBEN OTTENBERG, M. D.

The subject of leukemia is much confused at present.
None of the various theories has been generally accepted, and
the literature is full of inconsistencies and contradictions. It
is not clear whether leukemia belongs to the class of tumors
or to the class of infections, nor is it even clear whether all

cases of leukemia represent one disease. I will present a few
observations and experiments, without, however, drawing any
theoretical conclusions.

Many supposed protozoan blood parasites have been de-
scribed, but none of them has been confirmed. A list of those
described up to the date of its publication is given in Dr.
Ewing's "Clinical Pathology of the Blood." I have searched
for several of the most recently published parasites. Löwit's
bodies I have looked for (using the stain advised by Löwit[1])
in the blood of one case of acute leukemia; the result was nega-
tive. I have also failed to find the spirochetes recently reported
by White and Proescher[2], as occurring in the organs in leuke-
mia and certain allied conditions.

Probably all of the many bacterial infections reported as
occurring in leukemia and by some regarded as of etiological
significance are secondary. (Schultz[3] gives an account of many
of these.)

Auer[4] in 1903 observed certain peculiar structures in the
large lymphocytes of a case of acute leukemia. The granules,
crescents and rods which he described were seen both in the
fresh blood and in smears stained with various azur dyes or
with triacid mixture. The observations have been confirmed
once in the literature (by Pappenheim[5]).

I wish to demonstrate Auer's rods in the blood of three
cases of acute leukemia, and to report some experiments made
in the hope of throwing light on the nature of these rods. Auer
described three kinds of structures in the cytoplasm of the large
lymphocytes—granules, crescents, and rods. Of these the first
two are indistinguishable from the azurophile granulations now
recognized as occurring regularly in lymphocytes. The rods, on
the other hand, have a distinct and characteristic appearance.
They are found only in one place—in the cell body of the large
lymphocyte. Generally they are single, sometimes two are seen.
In preparations stained by Giemsa, Wright, or Hastings' method
they are red and remind one of the appearance of tubercle
bacilli. Generally they are a little longer and more slender

than the latter. Sometimes they seem nodular; generally the
ends are tapering, sometimes abrupt.

Of the three cases presented I have seen only one myself.
The other two were studied from smears in the blood collection
of Dr. Libman. One of these two cases proved at post-mortem
examination to be a case of chloroma.

The one case which I had an opportunity to follow was a
typical case of acute lymphatic leukemia of the rapidly fatal
type, with suppuration of the jaw, high fever, and multiple
hemorrhages. The leucocytes varied between 170,000 and 225,-
000 and the percentage of large lymphocytes was between 75
and 85 per cent. Two blood cultures were negative. Cultures
from the jaw during life and from the spleen post-mortem
showed Staphylococcus aureus.

The rods were examined from day to day. They were
never present in anything like the large numbers in which they
occurred in Auer's case (often four or five in a single micro-
scopical field). It was generally necessary to examine one hun-
dred to six hundred cells, in order to find a rod. No especial
connection could be made out (such as there was in Auer's
case) between the number of rods and the hemorrhages. On
two days no rods at all were found (as also happened in Auer's
case).

In the other two cases, likewise, the rods were present in
small numbers only. In studies of this kind the control obser-
vations are of great importance. Do these rods occur in the
lymphocytes in any other disease, or in health? I have examined
the blood of many normal subjects, both infants and adults, as
well as of many other types of disease, including myelogenous
and chronic lymphatic leukemia. No rods were found. It
should be remembered, however, that in the three cases of leu-
kemia in which the rods were found, it was necessary generally
to search through several hundred large lymphocytes in order
to find a rod. In acute lymphatic leukemia this was easy, but
in normal blood or the blood of other diseases the large lympho-
cytes form so small a proportion of all the cells that it takes

hours to see as many cells of this variety as can be seen in a
few minutes in a case of acute leukemia.

The interpretation of these rods is difficult. They might
be regarded as: (a) artefacts; (b) cell secretions, (c) parasites.

That they are artefacts can be excluded. They have been
seen in the fresh blood (Auer and Pappenheim). They occur
only in one type of cell and only in one place in that cell; and
they can be stained by a number of different methods. They
have a definite and regular size and shape. Whatever they are,
they are real.

The question as to whether these rods are products of cell
activity can not be answered definitely at present. They may
possibly belong to the same order of things as the azurophile
granules seen in many lymphocytes. They may be crystals.
(They, of course, have nothing to do with Charcot crystals,
which as is well known,[6] occasionally occur not only in the tis-
sues but in the blood of leukemia.) The fact of their occasion-
ally being found in vacuole of the cell body is rather in favor
of their being of a secretory or excretory nature. They are not
likely to be products of cell disintegration, as they are usually
found in well-preserved cells.

There is no proof that these bodies are parasites. Attempts
made to cultivate them, from the blood of the patient, on agar,
bouillon, ascitic fluid and sodium citrate, were all negative. As
the leucocytes in these nutritive media degenerated and lost their
staining power, the rods also disappeared. It was hoped that
some evidence on this question might be obtained from the
organs post-mortem, but examination of smears from spleen,
bone marrow, lymph nodes, and other organs failed to show the
rods or anything like them. (Auer did not obtain an autopsy.
Pappenheim does not state in his description whether the bodies
were found in the organs post-mortem or not.)

An effort was made in one other way to throw some light
on the question, namely, by inoculation. There have been many
unsuccessful attempts at inoculation of leukemia, not only from
man into the lower animals, but from man to man (Schupfer[7])

and from dog to dog (Weil and Clerc⁸). Recently Ellermann and Bang⁹ have reported the successful inoculation of the true leukemia of the fowl, and its transmission through several generations of fowls.

In the present experiments macacus monkeys were chosen. One monkey received intravenously fifteen cubic centimeters of blood drawn directly from the patient. The other received in the same way ten cubic centimeters of spleen pulp from the same patient post-mortem. Both monkeys have been kept under observation for six months and have apparently remained healthy. The blood of both monkeys has been examined frequently and has at times shown a marked relative lymphocytosis, small lymphocytes predominating. The experiments are to be regarded as negative, and it seems probable that leukemia, like malignant tumors, can not be inoculated from one species of animal into another.

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FOUR CASES OF ACUTE HEMORRHAGIC PANCREATITIS, ASSOCIATED WITH FAT NECROSIS.

BOWMAN C. CROWELL.

(*Assistant in Pathology at Bellevue Hospital.*)

Since Fitz in 1889 described the condition of acute hemorrhagic pancreatitis, an abundant literature on the subject has accumulated, and much excellent experimental work has been

reported, the latter having been an attempt to clear up the eti-
ology of the condition. However, the number of cases in hu-
man beings which come to autopsy is not as yet so great as to
preclude their presentation, in the hope of at least furnishing
further data for future investigators.

The chief problems to be solved in this condition seem to
be related to the etiology, and numerous theories have been
evolved to explain the manner in which the condition arises.
The series of cases which I am to present demonstrates that
Opie's theory of obstruction at the duodenal orifice of the com-
mon bile duct by calculi and the passage of bile into the duct
of Wirsung cannot explain all cases. Another hypothesis is that
of Thiroloix, who notices the frequent association of cholelithi-
asis and claims a common bacterial cause for gall-stones and
acute pancreatitis, the pancreatic lesion being set up, according
to this author, by lymphatic transmission of bacteria from gall-
bladder to pancreas. The evidence produced to uphold this doc-
trine seems somewhat open to question. Other possibilities are
infections travelling down the bile ducts and up into the pan-
creas, or from duodenum to pancreas. That intestinal contents
can be forced up into the pancreas only with the greatest diffi-
culty has been demonstrated in the dog, and Pearce's report of
a case of gastro-pancreatic fistula without acute pancreatitis
seems to demonstrate that gastric juice alone will not cause the
lesion. The production of fat necrosis has been proven experi-
mentally by Flexner, Opie, and others to be due to the action of
the fat splitting ferment of the pancreas. As Wells has pointed
out, this fat necrosis differs from simple necrosis in sharp limi-
tation of the affected area, by a wall of leucocytes and later of
connective tissue, and by the filling of the necrosed cells by the
products of fat splitting, lime salts being frequently deposited
in the necrotic areas in the process of healing. It is interesting
to note that this process in no way differs from that which
Klotz has described as occurring in sclerosing vessels.

The first case presents in brief the following features:
Three days previous to death the patient had sudden abdominal

pain and distention, with rigidity. There was slight fever, and the pulse rate varied from 90 to 120. He was operated on, and the diagnosis made. At autopsy he was found to be a large, well nourished male of twenty-nine years. There was no free fluid in the abdomen and no peritoneal adhesions were present. The omentum was large and fatty, but without evidence of fat necrosis. The heart, kidneys and liver were the seat of acute parenchymatous degeneration. In the liver there were also numerous subcapsular hemorrhages and the congested lungs were the seat of a bronchopneumonia. The alimentary tract and other viscera, except those to be described, were normal. Fat necrosis was seen in the pancreas, and peripancreatic, periportal, and perirenal fat. Hemorrhagic infiltration was present in the peripancreatic and perirenal tissues.

The pancreas was enlarged, especially in its head and body. The head was enlarged, brownish, soft, and greasy. The body was firm, pink, and fleshy in appearance, while the tail showed extensive hemorrhagic infiltration and fat necrosis. The interlobular septa were thickened, greyish, and necrotic in appearance. The pancreatic duct was of normal caliber, contained brownish yellow fluid, and opened in the ampulla separately from the common bile duct. The gall-bladder was distended and contained dark, tarry bile. The cystic, hepatic, and common ducts were of normal caliber and appearance, no calculi being anywhere present. The mucosa of the duodenum was bile stained and the mesenteric lymph-nodes small and pale.

The second case was one of an obese male of forty-eight years, who was found to have extensive arteriosclerosis, fibroid myocarditis, congested lungs, fatty liver, and normal kidneys and gastrointestinal tract. There was no free fluid in the abdomen. Numerous foci of fat necrosis were found in the mesocolic, omental, peripancreatic and peritoneal fat. The pancreas was enlarged and the seat of necrosis and hemorrhagic infiltration. The pancreatic duct was patent and of normal caliber, as were also the cystic, hepatic, and common bile ducts. The gall-bladder contained one calculus, 15 mm. in diameter, adherent

to its fundus, and some bile. There was no apparent obstruction to the outflow of either bile or pancreatic secretion, no dilatation of the ducts, and no evidence of a calculus having passed through them; nor was a calculus found in the intestine.

The third case was that of a very obese male of sixty years, who clinically presented the symptoms of sudden severe abdominal pain and distention, icterus, ileus, collapse, glycosuria and death in thirty-six hours from the onset of pain. At autopsy the obesity and jaundice were remarkable. The heart showed slight hypertrophy, and some early sclerosis of the coronary arteries and aorta. The lungs were emphysematous and congested, with a few synechiæ at the right apex, and one peritracheal node was calcified. The spleen was atrophic, and the splenic and superior mesenteric veins were the seat of recent thrombi, the portal vein being free. The liver and kidneys were the seat of acute parenchymatous degeneration. There was a considerable distention of the abdomen by a large amount of hemorrhagic fluid, in which oil droplets were visible.

The extent of the areas of fat necrosis was most remarkable. These areas were present in the parietal subperitoneal fat, in the omentum, perirenal fat, the peripancreatic fat, the pancreas, and the appendices epiploicæ in enormous numbers, varying in size up to a diameter of 4 mm. They were circular, definitely circumscribed, yellowish white to white in color, and pasty; and some were surrounded by a definite narrow circumscribing hyperemic zone. There was a considerable hemorrhagic infiltration of the abundant peripancreatic and perirenal fat.

The pancreas was enlarged to nearly three times its normal size, and its surface was reddish and brown in color, showing considerable hemorrhage. Section of the gland showed it to be of reddish brown color, with extensive hemorrhagic infiltration, and marked softening throughout, except for a small area in the middle part of the head of the gland where the normal appearance was preserved. Areas of fat necrosis were distributed irregularly throughout the gland. Dissection of the duct of Wirsung showed it to be somewhat distended, opening

into the papilla of Vater 7 mm. from its apex, its mucosa not pigmented. Impacted in the ampulla was a gall-stone 7 mm. by 5 mm., yellow and firm; and another smaller, soft, black pigment mass about 5 mm. long. The opening of the duct into the duodenum readily admitted a 2 mm. probe, the ampulla being 18 mm. in circumference, a considerable dilatation. The common, cystic, and hepatic ducts were dilated, but contained no other calculi except for one within the liver. The gall-bladder at its fundus was adherent to the liver, and was found to contain numerous gall-stones, the largest being spherical and 3 cm. in diameter. On section it was found to have a cholesterin center and cultures from it were sterile. Smaller pigment masses were also present and a very small amount of greenish turbid bile. The mucosa of the duodenum was bile-stained, and about 2 cm. above the opening of the papilla was found a small teat-like mass with central umbilication which was suspected to be the opening of the duct of Santorini, but on section this proved not to be so.

The last case was one of a woman of thirty years, who was admitted to the hospital markedly alcoholic, with the history of six weeks' illness at home with little or no attendance, during which time she had consumed enormous quantities of whisky. On admission she was without fever, with feeble rapid pulse, cyanosis and marked prostration. Soon after admission she went into profound shock, had marked abdominal distention, and constipation, and died forty hours after admission. At autopsy, performed by courtesy of Drs. O'Hanlon and Larkin, she was found to be a woman of small frame, and very poor nutrition, without evidence of icterus. There was no free fluid in the abdomen. Numerous typical areas of fat necrosis were found in the sub-peritoneal fat anteriorly, in the omentum, in the pelvis over the bladder, in the perirenal fat, in the peripancreatic tissues and in the pancreas. In the thorax these areas were also present in large numbers in the tissues of the anterior mediastinum, and completely covered the parietal pleurae, being most marked on the left side. In the left pleural sac was

a large amount of red clotted blood, and clear serous fluid. The lungs showed some congestion of the lower lobes, the heart a marked brown atrophy, the liver fatty infiltration, the kidneys acute parenchymatous degeneration; the spleen was normal and the vagina was the seat of slight ulceration. There were no venous thromboses. The duodenum contained some bile-stained mucus, and considerable pressure on the gall-bladder was necessary to force bile through the papilla. On dissection all the bile-ducts were found normal in caliber and appearance, and no concretions were anywhere present. The gall-bladder contained a considerable amount of dark bile, with some mucus.

The pancreatic duct opened into the papilla beside the common duct, just within the duodenal orifice, so that the common duct and duct of Wirsung could not be converted into one channel by any mass in the papilla. The duct of Santorini was not found. The pancreas itself was enlarged to about twice its normal size and was distinctly firm; and numerous red patches were distributed over its surface, with a few small areas of fat necrosis between the lobules. On section it was of good consistence, the pancreatic tissue being pale, yellowish, firm, with fairly numerous areas of fat necrosis distributed throughout the interlobular tissue, and hemorrhagic areas which were of variable size, being particularly numerous about the periphery of the gland.

Thus we have four cases, two of which are associated with cholelithiasis, one of these fulfilling Opie's requirements. Three of them occurred in obese males between the ages of twenty-nine and sixty. The clinical features are remarkably similar, consisting essentially in sudden pain and distention of the abdomen, collapse, symptoms of ileus, coma, and death. If gall-stones are present, icterus may be marked. In the fourth case, with a history of prolonged illness, the fat necrosis had extended into the thorax, probably by lymphatic transmission.

In all, the histology is similar, consisting essentially of widespread necrosis of the gland, involving parenchyma and interstitial tissue, inflammatory exudate, serum, and leucocytes,

and extensive hemorrhages. This hemorrhagic infiltration takes place not only in the pancreas, but in far distant parts as the perirenal fat, and in one case the pleura.

Discussion.

DR. E. L. OPIE agreed with the statement that some cases of acute hemorrhagic pancreatitis were not caused by gall-stones; the cases reported undoubtedly demonstrated this fact. Among Dr. Crowell's cases one-half were associated with gall-stones. Dr. Opie said that he had had the opportunity of see-ing seven cases; of these five were associated with gall-stones. In two cases gall-stones were found at the orifice of the diverti-culum of Vater. In four cases the gall-stones in the gall-bladder were numerous and of uniformly small size. It was certain that the proportion of cases of hemorrhagic pancreatitis with gall-stones was far greater than the proportion of gall-stones in individuals dying during the period of life when hemorrhagic pancreatitis occurred, although a contrary claim had been made. According to the statistics of Mosher, in individuals dying be-tween the ages of twenty and sixty, the proportion of gall-stones was about nine per cent.; whereas, according to Egdahl, the proportion in cases of acute pancreatitis was at least forty per cent. There was no doubt that a considerable variation of con-ditions might produce the hemorrhagic lesion. Experimental evidence lent weight to this view. A great number of irritating substances injected into the pancreatic duct produced the lesion in animals, notably certain acids, alkalies, gastric and duodenal contents, and formalin, as well as certain bacteria when injected in large quantities. Ligatures about the pancreas, shutting off the circulation, would produce the lesion and associated with it would be a fat necrosis. Such facts showed that various in-juries might produce the lesion. After the injury perhaps the trypsin of the pancreas produced the extensive necrosis of pan-creatic tissue peculiar to the disease. Necrosis of fat was pro-duced by the fat splitting ferment of the pancreas. With these

facts in view it seemed possible that conditions which obstructed
the blood vessels of the pancreas might produce hemorrhagic
lesions; the formation of thrombi as the result of injury might
explain the hemorrhagic pancreatitis which undoubtedly oc-
curred in a certain number of cases immediately after injury.
Dr. Opie said that it was not inconceivable that duodenal con-
tents might enter the pancreatic ducts, and produce hemorrhagic
pancreatitis. He believed that a considerable number, perhaps
the majority, of the cases were produced by the entrance of bile
into the pancreatic ducts; but there were undoubtedly other causes
which could also produce the lesion.

Dr. James Ewing called attention to Dr. Fitz' conclu-
sions, that, in cases of arteriosclerosis, rupture of blood vessels
formed an etiological factor in hemorrhagic pancreatitis. In
the case reported by Dr. Crowell this factor, he thought, might
enter.

Dr. B. C. Crowell said that the case was not associated
with arteriosclerosis alone. Arteriosclerosis itself, with rupture
of the blood vessels, was not sufficient to explain the marked in-
flammatory lesions present and the disturbances which followed,
and the necrosis was more marked in the interstitial tissue than
in the parenchyma. It was a question in his mind whether
arteriosclerosis could cause the condition.

A REPORT UPON THE VALUE OF NOGUCHI'S RE-
ACTION ON SPINAL FLUIDS.

C. K. STILLMAN, M. D.

The following report on the Noguchi reaction covers ob-
servations made in a series of thirty-one cases. We shall make
no attempt to consider the subject from the viewpoint of the
physiological chemist, but shall content ourselves with a short

résumé covering simply the result of the test in each case with reference to the clinical or post-mortem findings.

For purposes of analysis we may group our material as follows:

CLASS I. Tests on cases during life and uncontrolled by autopsy.

CLASS II. Tests on cases during life which were afterward controlled by autopsy.

CLASS III. Tests on spinal fluids obtained at autopsy.

The technique employed was that described by Noguchi.[1]

Class I, of cases in which the spinal fluid was tested ante-mortem only, contained eighteen cases. As no autopsy was made in any of these, a fair margin of error must be allowed for. While there is generally little difficulty in determining the presence or absence of lues in young infants by the clinical evidences, in adults we are often on less certain ground in excluding syphilitic infections.

We shall, for present purposes, have to consider as non-syphilitic those cases in which syphilis is denied and the accepted clinical signs are absent, and include as probably non-syphilitic, cases in which the history is unobtainable or unreliable, and which show no clinical evidences of syphilis.

Let us first consider those cases known to be actively syphilitic. Of these there were but two, a tertiary syphilitic twenty-seven years of age, who had had but two months' treatment following his initial lesion, and a case of congenital syphilis in an infant. In the first there was neither opalescence nor precipitate visible after standing considerably over the required time, and the test was therefore negative. The second, which also gave a negative Noguchi, gave a positive Wassermann reaction.

Of the non-syphilitic cases, eleven in number, two were cases of lobar pneumonia and one of these was complicated by alcoholic cerebral edema. Both gave negative Noguchi reactions. A Wassermann tried on the uncomplicated case men-

[1]Journal of Experimental Medicine, 1909, xi. p. 84.

tioned above was also negative. A case of bronchopneumonia
with chronic alcoholism gave a negative Noguchi. A fourth
case, a sacral abscess, gave a negative Noguchi and a negative
Wassermann. Six cases of tuberculous meningitis in patients
of varying ages all gave positive Noguchi reactions. On one of
these there was a negative Wassermann. A case of pneumo-
coccus meningitis in a child of six months gave a positive No-
guchi.

This series of positive reactions in seven consecutive cases
of meningitis seems worthy of attention.

There are five cases which are "probably non-syphilitic."
These include negative Noguchi reactions on four cases as
follows:

1. A case of chronic alcoholism and alcoholic psychosis;
2. Alcoholic wet brain; 3. Alcoholic pneumonia; 4. Multiple
sclerosis with negative history and clinical signs.

The one positive reaction was in a case of pyelonephrosis
with uremia. As this patient was admitted to the hospital in
coma, it would be unfair to lay any emphasis upon it.

An interesting feature so far has been the absence of a
reaction in the five cases of chronic alcoholism cited.

The complete summary follows:

CLASS I.

(a). ACTIVELY SYPHILITIC.

CASE XXII. Age 27. Tertiary Syphilis. Noguchi negative.

(Abstract of case.) Patient had chancre eight years ago with second-
ary manifestations following, and was under treatment at that time for two
months. Later he developed tertiary manifestations, including a syphilitic
orchitis and gummata in the temporal regions. He was recently an inmate
of Pav. A., Ward 1, Bellevue Hospital, suffering from gummata of the
head, where he markedly improved under large doses of potassium iodide,
with occasional doses of mercurial salicylate and calomel.

CASE XXIII. Infant, age 2 months. Congenital Syphilis. Noguchi nega-
tive. (Wassermann.)

(Abstract of case.) One of a family of five children, of whom one is
blind and another paralyzed. The most marked signs of syphilis included:
1, snuffles; 2, mucous patches in mouth and on buttocks; 3, desquamation
on forehead, palms of hands and soles of feet; 4, a coppery macular erup-
tion about the anus and on flexor surfaces of legs; 5, excoriated and fis-
sured lips; 6, greatly enlarged liver and spleen; 7, general glandular en-
largement.

This child is still in the hospital and is receiving calomel gr. 1/10
t. i. d., with salicylate of mercury, gr. 1/3, every third day.

	Noguchi	History	Clin. Signs
b) Non-Syphilitic			
Case XXXI, Adult ...... Lobar Pneumonia	— (Wassermann)		—
Case XVIII, Adult...... Lobar Pneumonia .... Alc. Cerebral Edema	—		—
Case XV, Adult......... { Bronchopneumonia .... / Chr. Alcoholism	—		
Case XXX, Adult........ Sacral Abscess........................	— (Wassermann -)		
Case XXXIV, 2½ yrs. . Tbc. Meningitis	-		
Case XIX, 15 mos. ...... " "	-	—	
Case XX, infant .... " "	-		
Case XXIII, 16 mos... " "	-		
Case XXIX, Adult ...... " "	-	—	
Case XXXII, Adult ...... " "	+ (Wassermann -)		
Case XIII, 6 mos. .... Pneumococcus Meningitis..............	-	—	

		Syphilis	
c) Probably Non-Syphilitic.	Noguchi	History	Clin. Signs
Case IV, Adult......... Chronic Alcoholism and Alcoholic Psychosis,	—	X	—
Case XI, Adult.......... Alcoholic Wet Brain.................	—	X	—
Case VIII, Adult....... Alcoholic Pneumonia (Lobar)...... ...	-	Cured Syphilis	—
Case XIV............... Pyelonephrosis and Uremia.............	-	X	—
Case XXI............... Multiple Sclerosis, ...	—	(Denied)	—

NOTE X History unattainable.

Class II consists of only two cases, both of which were non-syphilitic. The first, a case of pulmonary tuberculosis, gave a negative Noguchi and a negative Wassermann. The second, a case of adenocarcinoma of the stomach, admitted in coma, was at first suspected of being a paretic. Subsequent histological observations showed no lesions in the meninges or blood vessels that might be interpreted as syphilitic. This patient's spinal fluid was tested both ante-mortem and post-mortem, and a flocculent precipitate was obtained in about ten minutes in each instance.

SUMMARY OF CLASS II.

		Noguchi		SYPHILIS	
				CLIN.	ANAT.
Case XXVIII, Child....	Pulmonary Tuberculosis......	Antemortem —	(Wassermann —)	—	—
Case II, Age 69.........	Adenocarcinoma of Stomach..	Antemortem +		(Admitted in Coma)	—
	Senility...............	Post-mortem +			

There were eleven cases in which the fluid was tested post-mortem only. Of these, four were syphilitics, six were apparent non-syphilities, and one should properly be classed as doubtful.

The four syphilitic cases (in all of which the diagnosis was based on the anatomical data) included: 1. Juvenile paresis with status lymphaticus; 2. Syphilitic meningitis with lobar pneumonia; 3. Syphilitic proctitis with erysipelas; 4. Syphilitic cicatricial stenosis of the larynx with edema of the glottis.

The six apparently non-syphilitic cases included: three cases of chronic cardio-valvular disease, one cardio-nephritic, one carcinoma of the esophagus with lobar pneumonia, and a case of chronic pulmonary tuberculosis.

The case classed as doubtful was one of cirrhosis of the liver with acute parenchymatous nephritis.

In every case of the entire series of eleven, non-syphilitic and doubtful, as well as syphilitic, there was a well-marked Noguchi reaction.

The appended summary gives the findings in a concise form.

CLASS III. (Fluid tested at Autopsy)

Syphilitics.		Noguchi.	Syphilis.	
			History	Anat.
Syphilitics.				
Case V, Age 12......	Juvenile paresis, (4 hrs. P.M.)............. Status Lymphaticus	+	unobtainable	+
Case X (50)..........	Chr. Basilar Meningitis (Syph.) .... Lobar Pneumonia, (15 hrs. P.M.)...........	+	unobtainable	+
Case XII...	Facial Erysipelas .... Syphilitic Proctitis	+	(denied)	+
Case XVI............	Edema of Glottis .... Cicatricial stenosis of larynx	+	unobtainable	+
Apparent Non-Syphilitics.				
Case VI (39)..........	Chr. Cardio-valvular Disease............. Chr. Alcoholism, (6 hrs. P.M.)	+	—	—
Case XXIV (48)......	Chr. Cardio-valvular Disease, (18 hrs. P.M.)..	+	—	—
Case XVII (53)	Aortic Stenosis, (3 hrs. P.M.)	+	—	—
Case XXVI (50)......	Cardio-Nephritic, (10 hrs. P.M.)...........	+	unobtainable	—
Case XXVIII	Carcinoma of Esophagus............... Lobar Pneumonia, (24 hrs. P.M.)...........	+	—	—
Case IX (29)..........	Chr. Pulm. Tuberculosis	+	—	—
Doubtful				
Case III (53)..........	Cirrhosis of Liver.................. .... Acute Parenchymatous Nephritis	+	(denied)	(scars on tibiæ)

GENERAL SUMMARY AND CONCLUSIONS.

Our results may be briefly summarized as follows:

1. A positive reaction was constantly obtained in inflammatory conditions of the meninges.

2. Spinal fluids obtained post-mortem invariably gave a positive reaction.

In reference to the value of the test in diagnosing syphilitic conditions:

1. In two cases of syphilis, one congenital, the other tertiary, the spinal fluid failed to give a positive reaction. Both cases were under active treatment at the time.

2. In ten cases giving no history or clinical evidence of syphilis, a positive reaction was obtained twice.

The Wassermann and Noguchi tests were done simultaneously on five cases. They were in agreement three times out of the five.

Discussion.

Dr. Noguchi said that the findings of Dr. Stillman were highly interesting and appeared to be in harmony with his own, except in a few instances. These differences might be due, in part, to the method of reading the reactions. The negative results obtained with the specimens from syphilitic patients were probably due to the fact that the reactions there were usually weak and required a longer period of observation. The positive results with non-syphilitic, probably normal, cerebrospinal fluids taken from cadavers were to be explained by the assumption that the material was secured after general autolytic processes had set in and the fluid contained more or less serous effusion. According to Dr. Noguchi's observations on the specimens taken soon after death, normal spinal fluid never gave a positive reaction. The speaker further stated that the butyric acid reaction was simply an indication of the increase of abnormal protein fractions in the spinal fluid, and was always present in cases of meningeal inflammation of any kind. He considered, however, that when applied under certain conditions the butyric acid reaction was of great help in deciding doubtful diagnoses of metasyphilitic affections.

A MALIGNANT ADENOMA OF THE ADRENAL, WITH TRANSFORMATION INTO SARCOMA- TOUS TISSUE.

J. C. MEAKINS, M. D.

(*Resident Pathologist, Presbyterian Hospital, New York.*)

Malignant adenomata of the adrenal are uncommon, and especially uncommon are adenomata which show, in the primary tumor or in the metastases, sarcomatous transformation. Such a condition is paradoxical, but the embryology of the adrenal affords an explanation. It was formerly believed that the cortex of the adrenal developed from the mesoblast and the medulla from the epiblast. The studies of Janosik and Gottschau, Minot,[1] and Aichel[2] have established the fact that the entire adrenal develops primarily from the mesoderm. The mesoderm divides into two parts; the mesochymal part forms the connective tissues, and from the mesothelial part develop the serous membranes, the genito-urinary tract (except the urinary bladder) and the striated muscles. The mesothelial structures undergo greater differentiation than the mesochymal tissues and take on certain "epithelial" characteristics.

It may be assumed that the cells of a malignant tumor do not acquire new features, but revert to a former state; there is reversion first to the characters latest acquired, and finally to the original embryological condition. This view may help to explain peculiarities of the following case. Since the cells of the adrenal are mesothelial in origin and assume epithelial functions, tumors arising from them may exhibit epithelial characters of new growth, but revert to the primitive mesodermal type more readily than cells primarily of epithelial origin.

The patient with the tumor which will be described was admitted to the Presbyterian Hospital on January 6, 1908, in the service of Dr. Eliot. I wish to express my thanks to Dr. Eliot for permission to report the following facts concerning the history of the case.

The patient, W. N., was white, male, aged forty-five, and by occupation a letter carrier. His family history is unimportant. He was born in the United States, where he had always lived. Many years ago he had used alcohol in moderation; he had had gonorrhea in 1897. Otherwise his history contained nothing noteworthy.

In 1905 the patient had hematuria for a week without subjective symptoms. He remained in good health until December 24, 1908, when he noticed that his urine was dark brown. Three days later he developed, suddenly, severe pain in the left flank. It was not increased by deep respiration or by movement, but on assuming the right lateral position it was greatly increased No bright red blood was observed in the urine.

Physical examination revealed a prominence in the left flank and on palpation a large, tender tumor was found in this region. It disappeared under the costal margin and could be moved only in an antero-posterior direction. There was flatness from the fourth intercostal space to the crest of the ileum, and the splenic dulness merged with that of the tumor. When the patient assumed the right lateral position the tumor approached almost to the median line. The heart, lungs, and nervous system were normal. Blood examination showed no abnormality.

The urine was dark brown, acid, and had a specific gravity of 1020. It contained about 0.1 per cent. albumin, and no glucose. Microscopical examination revealed hyaline and granular casts, many red blood cells, leucocytes, and epithelium. Urea was 2.7 per cent. The ureters were catheterized, but the urine from the two sides was practically the same in character. The right kidney was excreting the greater amount.

On January 6, 1908, Dr. Eliot found at operation a large, firm, nodular mass, occupying the site of the left kidney. It extended from above the costal margin downward almost to the crest of the ileum. The tumor pushed the peritoneum forward and to the right, but was completely retroperitoneal. It was removed with great difficulty, and there was considerable hemorrhage.

Pathological Examination.—The specimen has the general shape of a kidney, measuring 18 x 11 x 10 cm. The outer part consists of a thick layer of perirenal fat in which are imbedded tumor nodules of various sizes. These tumors are yellowish white and very friable. They contain many blood vessels and into some of the nodules hemorrhage has occurred. Many of the larger masses seem to infiltrate the surrounding fat. This perirenal mass, although thickest at the upper pole, completely surrounds the kidney and is removed with little damage to the kidney substance.

The kidney measures 13 x 7 x 4 cm. The posterior surface is smooth and the anterior surface and the borders contain tumor nodules similar in character to those in the perirenal fat. After longitudinal section through the pelvis the kidney is found almost entirely replaced by new growth. The only part of the cortex which remains intact is upon the posterior surface of the organ. The tumor nodules might be divided into two varieties according to the color and consistency. One is white, more or less granular and very friable. The other is yellowish and firm. In some nodules the two varieties are combined and merge into each other. The white nodules exhibit a tendency to infiltrate the surrounding fat. Reference will be made later to this distinction.

Microscopical sections were made through different parts of the new growth and the changes which were found may be divided into two groups. In some sections the cells had the typical appearance and arrangement of adenoma, while in others the arrangement was sarcomatous.

Adenomatous Tissue.—The histological appearance presented by the tumor tissue of this type is entirely different from that observed in the sarcomatous areas. The difference is not so much in the character as in the shape and arrangement of the cells. The cells are cuboidal with a faintly staining protoplasm which is finely granular. The nucleus is usually situated near the periphery of the cell. It is round and vesicular, with

a deeply stained nucleolus and a pale chromatin network. These
cells closely resemble those of the adrenal cortex.

The cells in a single layer are arranged to form tubular
alveoli. The alveoli are usually straight, but occasionally are
tortuous. The lumina are patent and frequently contain debris,
derived from desquamated cells. Between the alveoli there are
fibrous trabeculæ fairly rich in cells. The reticulum is well
demonstrated by Van Gieson's stain, and does not extend be-
tween the tumor cells. Broad bands of connective tissue sepa-
rate the tumor into lobules and from these bands the trabeculæ
between the alveoli are derived. (Figure 1.)
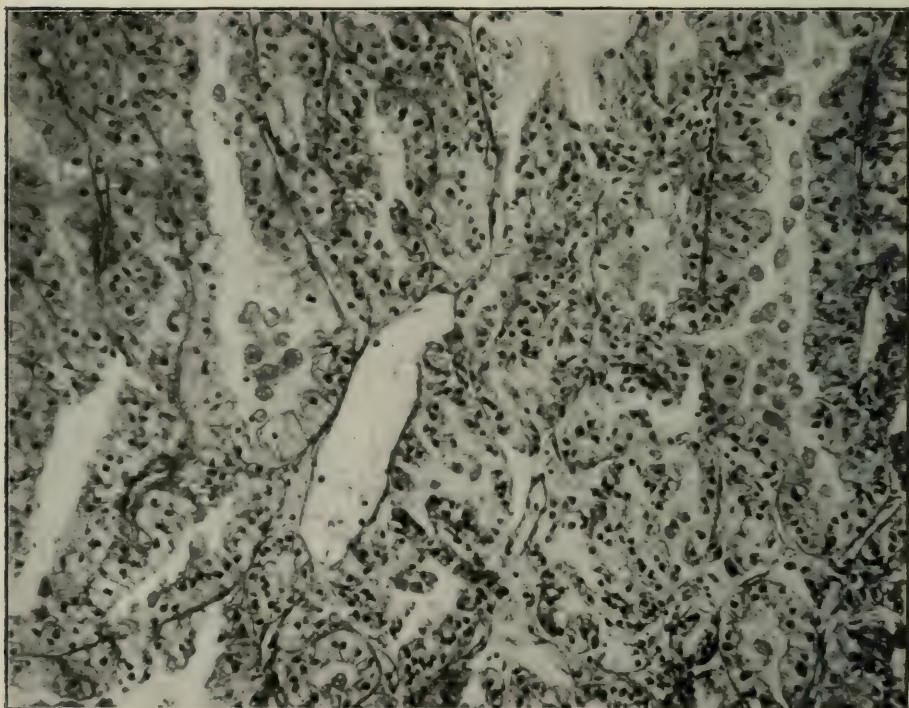
FIGURE 1

In some of the larger tumor masses of this type the cells
at the periphery of the mass differ from those in the center. In
the center the cells tend to lose their distinctly alveolar arrange-

ment. The lumen disappears and the trabeculæ become less distinct. The cells at the same time become longer, although the nucleus does not change.

Sarcomatous Tissue.—There are found in such parts of the tumor various types of cells which may be grouped in three classes. Some of the cells closely resemble those of the normal adrenal cortex. They have a large deeply staining nucleus, which, as a rule, is round, but occasionally assumes an oval shape. The cell body is small and, corresponding in shape to the nucleus, is round or oval. The protoplasm takes eosin poorly. These cells are not numerous nor uniformly distributed, but occur in small collections chiefly about the blood vessels. Under the low power of the microscope they closely resemble lymphocytes, but with a high magnification a difference is apparent.

Closely associated with these cells there are large spindle shaped cells which form the greater part of the tumors. The protoplasm of these cells stains poorly and contains fine granules and sometimes small vacuoles. The nucleus is large and, as a rule, is spindle shaped, but frequently it is irregular in shape. It stains poorly and has a fine chromatin network; there is a deeply staining nucleolus which is situated toward one end of the nucleus. Besides these cells there is a large irregular cell with a faintly staining, irregular nucleus. The cell body contains many vacuoles, some of which are large and appear to fill the whole protoplasm, displacing the nucleus.

A series of transitions between the three kinds of cells described above, indicates that they are all derived from the same source, namely, the cortical cells of the adrenal. Mitotic figures are very common and both regular and irregular types are observed. Multinucleated cells are frequently found, and the nuclei are usually arranged at the periphery of the cell.

In sections stained with Van Gieson's stain broad bands of connective tissue are found separating the tumors into lobules. In addition a few fine strands of reticulum are occasionally found between the cells, but, as a rule, the cells are closely packed together. This is especially true where the spindle cells pre-

dominate. These cells are arranged with their long diameters more or less parallel, but without any evidence of alveolar arrangement. (Figure 2.)
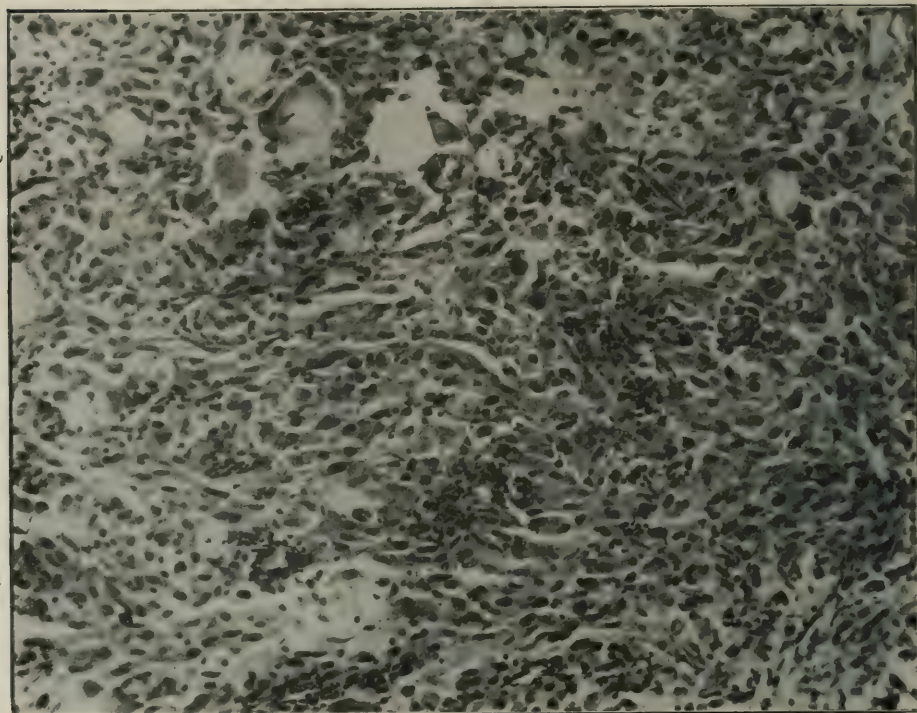
Figure 2

The blood vessels are abundant, and are in intimate contact with the tumor cells. In fact the walls of the veins in many places are formed by tumor cells covered by endothelium, and occasionally a vein is found whose lumen is invaded by tumor cells. A section through the vessels at the hilus of the kidney shows one of the smaller veins almost completely obliterated by a parietal thrombus. A mass of tumor cells found at the point of attachment of the thrombus appears to be the cause of the thrombosis.

The sarcomatous type of tissue is present alone in the

white, friable nodules described above, and is the predominating form of tissue in the perirenal mass, and these tumor nodules are invading the surrounding fat. In the kidney substance the nodules of this type are large and ill-defined, showing invasive characters. The yellowish nodules have the histological structures of adenoma and are circumscribed. In some of the tumor masses both white and yellow tissue is found, and in these nodules sarcomatous and adenomatous structures are side by
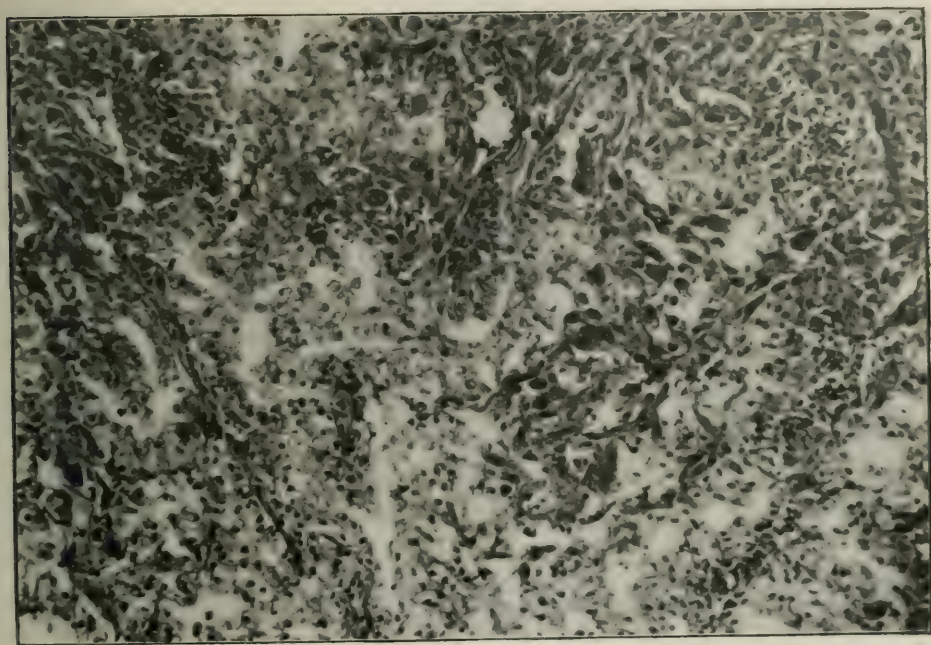
FIGURE 3

side. As a rule the two types are well isolated by bands of fibrous tissue; but in some places the adenomatous structures exhibit the loss of alveolar arrangement described above. The cells become spindle shaped and their nuclei take on an oval form and become paler; and a complete transition may be traced in the same tumor from a purely adenomatous structure to one with typical sarcomatous cytology and arrangement. (Figure 3.)

In accordance with the embryology of the adrenal all malignant tumors of the gland should be classed as sarcomata, but from the histology of the normal gland carcinomata might be expected to develop. In the present case the larger masses exhibit the cellular characters of sarcoma. There is, however, evidence to show that these tumors may have been originally carcinomatous structures, and as the growth progressed the reversion to the mesothelial or sarcomatous type of cells occurred. In fact such transformation or reversion is demonstrated in some of the tumor masses. If these tumors had had opportunity to continue their growth, reversion to sarcomata would no doubt have become complete.

Jores[3] has described a sarcoma of the adrenal in which a direct transition could be traced from the normal adrenal cells to the cells of the sarcoma. In this case metastases in the brain were of the same structure as the main tumor. In another case he describes an alveolar sarcoma which in places resembled slightly the histological structure of carcinoma. On the evidence afforded by these cases Jores believes that all malignant tumors of the adrenal are sarcomata, although they may resemble in some parts carcinomata.

Rolleston and Marks[4], after a careful study of tumors of the adrenal, make the following statement: "Our own impression is that malignant tumors of the suprarenal bodies are peculiar and form a special class. They may approach structurally either the carcinomata or sarcomata and sometimes one and the same tumor may in different parts resemble both."

Woolley[5] has reported a case in which a transition was demonstrable between the adrenal cells and a primary adenoma of the adrenal, accompanied by metastases, all of which were sarcomatous. He believes this condition is explained by the embryology of the adrenal and thinks that such malignant tumors should be called "mesotheliomata."

Such cases show that tumors of the adrenal may begin as sarcoma or as carcinoma and revert to a sarcomatous type of tissue. Such reversion may occur as a direct transformation

from the normal adrenal cells to sarcomatous or carcinomatous cells, or may occur in metastases from the original adenoma; or, as in my own case, may be by a series of transitions within the same tumor nodule.

I wish to thank Dr. Opie for his help and advice to me in this work.

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Discussion.

DR. E. L. OPIE said that this case was of some interest in connection with recent experimental observations. The yellow nodules undoubtedly represented the original tumor; the sarcoma-like change had occurred secondarily. The condition was not analogous to the transition from carcinoma to sarcoma found in experiments. In such tumors reproduced by inoculation, carcinomatous and sarcomatous elements appeared to exist side by side. In the tumor which had been described there was transition from one type of cell to another. It was, however, merely an apparent transition, for embryological studies suggested that mesothelial cells had taken on an epithelial character to form adrenal tissue, and might with tumor formation revert to the mesodermal type.

MALFORMATION OF THE TRICUSPID AND MITRAL VALVES, WITH AURICULAR COMMUNICATION IN AN ADULT.

A. K. DETWILLER, M. D.

This specimen was found in a plethoric male subject who died at the age of eighty-three years, of degenerative productive nephritis with general anasarca and fluid in the serous cavities. Unfortunately, a medical history and a written physical examination are lacking, as the patient was an inmate of the City Home. The only information we have relative to the heart is that the patient had a well-marked murmur, which was not described.

The body was that of a well-nourished man, rather obese, and of the short necked, thick set type. There was no clubbing of the fingers. The head and neck were livid with venous stasis.

On examining the heart, it was found to be large, weighing 565 gms. The right side was distended, the left ventricle firm and contracted, forming the apex. The tricuspid valve admits four fingers plus, and the mitral three easily. The average thickness of the right ventricle is 8 mm., that of the left is 12 mm. The heart muscle is pale brown in color, not friable, but very firm. The muscle bundles are easily differentiated and show considerable increase in connective tissue; the endocardium is smooth, but shows some fibrous thickening, this especially in the left ventricle. The coronary arteries show diffuse thickening with occasional calcareous patches. They were patent.

The left auriculoventricular ring measures 14.5 cm. in circumference. The tricuspid valve is well preserved and only slightly thickened. Its posterior, or septal, flap shows an abnormal opening, which has well defined edges and freely admits the finger. This is slightly to the right of the center of the flap and is nearer the margin than its attachment. Another mal-

formation is found further to the left, where this flap is at-
tached to the auriculoventricular ring.

In this location there is an equilateral triangular opening
with well defined, smooth, rounded edges. The apex of the
triangle is directed downward, and its sides measure .5 cm. This
aperture is 1.5 cm. directly below the site of the well closed
foramen ovale, and it renders the auricular septum incomplete
at this point by communicating directly with the left auricle.
Here it presents the same features and is in relation with the
attachment of the anterior flap of the mitral to the auriculo-
ventricular ring. The mitral ring measures 10.5 cm. in circum-
ference. The posterior flap is fairly well preserved and shows
some diffuse thickening; the anterior flap is greatly thickened,
owing to an atheromatous fibrous change with some calcareous
degeneration. This thickening, on being sectioned, measures
nearly 1 cm. at its greatest width. The attachment of this flap
is irregular at its aortic aspect, where several bar-like ridges
are formed. The endocardium is everywhere perfectly smooth.
The pulmonary cusps are well preserved and the valve measures
10.5 cm. in circumference. The aortic cusps show diffuse thick-
ening and calcareous deposits along their attachments. The
right posterior cusp shows a fenestration, and the left posterior
a fine fringe-like vegetation of its corpus arantii.

In seeking a cause for the defect in the auricular septum
the embryological development of the heart offers a more satis-
factory explanation than an endocarditis.

Aside from the malformations the heart is a remarkably
well preserved organ for a person of that advanced age. It
may be regarded as certain that this lack of closure is due to
imperfect fusion of the two processes which go to form the in-
terauricular septum. It seems unreasonable to attribute this
condition to either a fetal or an extrauterine inflammatory en-
docarditis, for the reason that evidences of a past destructive
endocarditis of a type which necessarily would have been re-
quired to produce such an opening are entirely lacking. But,
on the other hand, the previously described malformations of

the tricuspid and auricular septum decidedly favor a develop-
mental anomaly. Moreover, the situation of the lesion is such
that it lends itself most easily to a developmental explanation.

In the embryological development of the heart, the septum
of the common auricle appears as the upper and back part of
the auricular cavity. The free edge of this septum grows for-
ward and downwards, and the septum gradually separates the
auricular cavity into a right and left half, the separation being
completed by the junction of its free edge, which shows a dis-
tinct endocardial thickening, with the fused cushion-like thick-
enings, which are subdividing the common auricular orifice.
Here the development of the septum was deficient, probably
owing to the septum superius either being too short to complete
the gap or being prevented from fusing, owing to the rapid in-
terchange of blood through this aperture. A new opening now
makes its appearance before the originally free communication
between the two auricles closes. This new orifice, the
foramen ovale, above and at the back of this septum gradually
enlarges so that a passage is thus re-established. This becomes
closed by a second septum which also starts from the superior
auricular wall, a little to the right of the original attachment of
the first septum, and gradually grows forwards and downwards
over the orifice. Our opening, being well below the site of the
foramen ovale and in the exact location of this first communi-
cation, must certainly be due to imperfect closure or arrested
development at this point.

Had this occurred just a trifle lower, a communication be-
tween the ventricles would have resulted. This is a site where
defects in the ventricular septum most usually exist, namely, in
the uppermost portion of the ventricular septum, which is
termed the undefended or membranous part of the septum.

MULTIPLE ECHINOCOCCUS CYSTS OF THE LIVER AND PERITONEUM.

E. H. SPARKMAN, M. D.

E. P., male, an Italian, who gave his age as seventy years, but appeared about fifty-five, was admitted to the Second Medical Division* of the City Hospital, January 2, 1909. He complained of a painful swelling of the right groin.

Family history: Negative.

Personal history: Negative, except for a history of gonorrheal infection fifteen years previously.

History of present illness: First noticed the swelling in the right groin six months previous to admission, accompanied from the first by some pain. For two months he had noticed a yellowish color of his skin. In the two weeks previous to admission he had felt some pain in the right hypochondrium, and thought his abdomen had become larger during this time.

Physical examination: The patient was somewhat jaundiced and rather emaciated. The abdomen showed a moderate general enlargement. In the right upper quadrant was a globular protuberance, which was described as "less tympanitic than the rest of the abdomen." On the left, outside the nipple line and just above the level of the umbilicus, was a second, rather indefinite, but freely movable mass. A linear scar extended from just above the symphisis pubis to within 4 cm. of the umbilicus. In the lower end of the right inguinal canal was a mass about the size of an egg. There was also a small, hard nodule, about the size of a cherry, closely adherent to the lower surface of the right testis.

On January 20, the patient was transferred to the surgical division for the removal of this mass in the groin for examination. At operation the mass was found closely adherent to the spermatic cord and attached to the floor of the inguinal canal by a short pedicle. When this was cut through the peritoneal

*Service of Dr. C. C. Ransom.

cavity was found to have been entered. This mass proved, on examination, to be a typical hydatid cyst. Other cysts were found on the peritoneum in the vicinity of the wound. The operation was completed by the Bassini method.

A second operation was performed on January 26, the former incision being re-opened and enlarged, and a second incision made over the liver. A large hydatid cyst of the liver was opened and evacuated, a second large cyst occupying the lesser peritoneum was evacuated and a cyst involving the appendix and meso-appendix was removed. The contents of the two larger cysts amounted to two and one-half liters or more. The patient died the following day.

At autopsy the following condition was found: On opening the abdomen, there is a firm adhesion between the peritoneum and the liver, just above the operative wound in the right hypochondrium. The abdominal cavity contains no fluid. The intestines, with a slightly pinkish shining serosa, lie for the most part in the lower abdomen and pelvis, and occasionally show markedly dilated superficial veins. The large omentum is represented by a thin, very atrophic membrane, and lies curled up between the colon and the stomach, which, very much dilated, occupies the whole left hypochondrium to the umbilical region. The right hypochondrium and epigastrium are occupied by the liver, which projects 6.5 cm. into the left hypochondrium with its left lobe, the notch being about 7 cm. below the costal margin. The right lobe, however, lies high up, so that its edge does not come below the costal margin. The peritoneum as a whole is distinctly reddened and thick. In the right iliac fossa, immediately below the wound of the first operation, is a small globular body attached to the peritoneum by a short pedicle. A similar body is attached to the cecum. The cecum and ascending colon lie deep, surrounded by numerous old and recent adhesions and with considerable hemorrhagic inflammations. There are a number of firm adhesions between the under surface of the liver, the hepatic flexure, and the pylorus. In attempting to remove the hepatic flexure one cuts directly into a

large, thick-walled cyst cavity, which discharges considerable cheesy, gelatinous material and contains numerous variously sized, smooth, globular, pale, shiny, independent cysts. Below the stomach there is an opened cyst cavity of the same character, which passes directly under the pylorus and becomes attached to the under surface of the liver and to the mesentery. These cysts have been emptied by recent operative interference. The mesentery of the sigmoid flexure shows, in its lower portion, a number of large, smooth, globular masses, which, on incision, discharge independent cystic bodies similar to those already described. The liver is large and its right lobe is the seat of a cyst which contains gelatinous material, with innumerable cysts of all sizes and of the character previously described.

Intimately connected with, and occupying, the foramen of Winslow, is a sac filled with gelatinous, greenish, pale masses. To the right of the gall-bladder, which is distended, thick, and surrounded by adhesions, one strikes a large, open sac, which is continuous with the under surface of the right lobe of the liver, and the contents of which have been removed by operative interference.

Intimately connected with the larger cysts are a number of well circumscribed, smaller ones, which contain similar material. The fluid from these cysts was slightly turbid, almost colorless; specific gravity, 1.012; reaction faintly acid. With heat and acetic acid a very faint cloud appeared. A drop of silver nitrate caused a heavy precipitate. Fehling's solution was reduced, and rendered colorless with the formation of a black precipitate. The reaction for succinic acid was negative. Microscopically there were found cholesterin crystals, hooklets, scolices, and pieces of the characteristic laminated membrane.

Echinococcus cysts occur in three forms: First, the hydatid form, which consists of a single cyst in which there is an endogenous formation of daughter cysts, brood capsules, and scolices. (This form occasionally shows also an exogenous proliferation.) This is the Echinococcus hydatidosus, or Echino-

coccus altricipariens. This is the form most commonly found
in man.

Second, the Echinococcus veterinorum, or Echinococcus
scolicipariens, the form occurring most frequently in the lower
animals, in which there is a single cyst lined with brood cap-
sules; or, if daughter cysts are formed, they are produced exo-
genously. They may at times become invaginated and appear
to have been of endogenous origin.

Third, the Echinococcus multilocularis, sive alveolaris, in
which there is an alveolar, sponge like, frame work, containing
considerable lime salts, and in which are numerous independent
cysts. This form is rare in man, the total number of recorded
cases being less than 250. It is stated to occur, not infrequently,
in large cattle, rarely in sheep and swine.

The interesting features of the present case are the multi-
ple distribution of the cysts, and their variation in size and de-
velopment. On these points Leuckart offers some explanation.

The variation in size and development may occur, as he
suggests, in three ways: First, by repeated infections with the
ova of Tænia echinococcus. He regards this, however, as very
infrequent, arguing that inasmuch as echinococcus infection is
in any event rare, repeated infections in the same individual
must be still more so.

Secondly, he says, must be considered the possibility of the
smaller cysts developing by the proliferation of the larger ones,
but he holds, in this instance, that the young brood always de-
velops in the immediate vicinity of the older and larger cysts.
This would be an example of exogenous proliferation, and has
been observed even in cysts of an endogenous type. This is
rare, however; and I do not regard the present case as an ex-
ample of exogenous proliferation, for all these cysts, even the
smaller ones, contain daughter cysts.

Thirdly, he suggests that, when smaller and larger echino-
coccus cysts are formed at some distance from each other, or
even in distant organs, it is very probable that, of a number of
embryos introduced simultaneously, some have met with condi-

tions more favorable for their growth and development, and consequently have outstripped the others. This explanation is, in my opinion, the most applicable to the case before you; for one finds here cysts in which development either has been very slow or has ceased; e. g., the small cyst found near the inguinal wound, a similar one near the cecum, and those found along the sigmoid flexure. Another point which bears out this contention is the fact that daughter cysts have, not infrequently, been found free in the peritoneal cavity.

Leuckart refers to this point again in discussing the cause of the multiple occurrence of the cysts. He draws attention to the conditions under which the parasites develop, as well as the number of parasites that gain entrance as points to be considered, and believes that the same number of parasites may in one case produce multiple cysts, and in another case but one cyst. In the latter case the single parasite may have been a "hermit" from the first. Or, on the other hand, though a number of parasites gain entrance simultaneously, one of them may find better conditions for existence, such as nutrition, and, by its more rapid growth, may outstrip the others and finally overgrow them. The fact that such overgrown, retrograde cysts were formerly very rarely encountered can hardly be taken for ground for opposition to this view, if we reflect that echinococcus disease usually comes under our observation only after several years' standing. Leuckart emphasizes the selective affinity of the parasites for certain structures, in which they develop in greater number than in other situations. While, for example, more than five or six cysts are rare in certain organs, as in the liver or lungs, in the peritoneum and omentum the occurrence of multiple cysts is so frequent that the isolated cyst in this locality becomes almost an exception.

Finally, while the exact manner in which the embryos find their way into various localities, whether by blood-stream or lymphatics, or by directly boring their way, is still a mooted question, the large surface of the peritoneum easily offers a chance

for simultaneous invasion by a considerable number of embryos, and the opportunity for subsequent independent development.

In conclusion, I will say that I regard this case as an example of a simultaneous invasion of a considerable number of parasites, in which varying conditions of nutrition are accountable for their extreme variations in size and development.

Discussion.

DR. N. B. POTTER said that at the French Hospital he had had a case of hydatid cyst of the liver which had suppurated, and on which Dr. Peck had operated. The tumor had pushed the heart up and out, so that the apex was in the anterior axillary line in the fourth space. This was the second case he had seen since he had been in New York. The disease was formerly quite rare in America, for, in 1901, Lyon had been able to collect from American literature only two hundred and forty-odd cases.

REPORT OF CULTURES OF TUBERCLE BACILLI ISOLATED FROM MILK.*

ALFRED F. HESS, M. D.

In an examination of the milk supply of New York City, made by me over a year ago, seventeen samples, among 107 of milk retailed from forty-quart cans, were found to contain tubercle bacilli. A full report of this study, together with a consideration of the welfare of the children who drank this contaminated milk, has been published elsewhere. In the course of this work it was considered that it might be of interest to isolate some of these strains of tubercle bacilli, and to determine their cultural and pathogenic characteristics. It was to be expected,

considering the source of the material, that probably all of the
strains would prove to be bovine in type. However, there
seemed a possibility, owing to the great degree of exposure to
which such milk is subject in its journey from the cow to the
retailer, that contamination with bacilli from human sources
might occur. In the hope of encountering such a case, cultures
were undertaken. It seemed also of interest to inquire whether
the cultures would conform strictly to definite types or whether
intermediate varieties, such as have been met with by some
others, would be isolated.

The technique employed was, in brief, as follows: Ten c. c.
of milk was centrifuged, and 1 c. c. of the cream injected into
a guinea-pig. One c. c. of the lowest skimmed milk was in-
jected into another guinea-pig. In some cases one of these
pigs developed tuberculosis; in other instances, both of them.
Of the cultures which I now report, five were made from
guinea-pigs inoculated with cream, three from animals inocu-
lated with sediment. I shall not detail the method of obtaining
cultures, as it is the one generally in use, and similar to that
employed by me in previous studies.

In some cases coagulated dog serum was used as medium,
as first suggested by Theobald Smith; but in most instances the
tissue was transferred directly to Dorset's egg medium. In two
instances, not included in this series, culture was attempted, but
failed; in two others the growth was very scanty and after the
third generation the strain was lost.

The results are given in the appended table. A review of
this summary shows that seven cultures induced a fatal general-
ized tuberculosis in the rabbit, whereas one possessed but slight
virulence for this species. For these tests intravenous inocula-
tions of standard emulsions were employed, excepting in the
last case, where, it will be noted, 1 mg. of culture was inocu-
lated. This strain was isolated and studied by Dr. Woglom and
Dr. Krumwiede, whom I take pleasure in thanking for this
work.

Cultures I to VII must be classed as bovine in type, not

only on account of the marked virulence to rabbits which they
exhibited, but also on account of their cultural characteristics.
They grew very sparsely, showing for some generations only a
fine veil-like growth, which it was very difficult or impossible to
transfer successfully to glycerin bouillon. They were markedly
similar in all these properties, only one standing apart from the
others, in that it showed a more abundant growth in the first
generation. However, even this strain did not grow profusely
when compared with cultures of the human variety.

Culture VIII is of especial interest and seems worthy of
detailed description. The original material was obtained from
a can of milk in a small grocery store. It was inoculated sub-
cutaneously into two guinea-pigs, both of which developed gen-
eralized tuberculosis. From one of these animals, tissue was in-
oculated into another guinea-pig, from which cultures were
made upon egg media about two months later. In order not to
lose the material, tissue was once more transferred to a pig, and
further cultures carried out after the same interval. These two
sets of cultures proved to be identical; after three weeks a vig-
orous confluent growth was obtained on glycerin egg. These
results were so unexpected that a rabbit was inoculated with one
of these strains, and cultures were made from its tissues. By
using the rabbit instead of the highly susceptible guinea-pig we
made certain of selecting for culture the most virulent bacilli.
These strains grew vigorously, in a manner characteristic of
bacilli of the human type. Reference to the virulence tests of
the table shows that this strain (Culture VIII) in strong con-
trast to all the others, possessed but feeble virulence for rabbits.
One of the rabbits when inoculated weighed 1,740 grams, and
when killed had gained 550 grams; the other weighed 1,710
grams and after a period of sixty-three days weighed 1,820
grams. Thus, this culture in contradistinction to the others
must be regarded as belonging to the human type, on account
both of its facility for cultivation and of its comparatively feeble
virulence.

From a study of these eight cultures we must emphasize the

sharp contrast which usually exists between tubercle bacilli of the human, and those of the bovine type, a distinction which in the instances here reported was absolutely diagnostic and incapable of misinterpretation. Furthermore, the results are instructive from another point of view; for, for the first time, they bring forth an instance where tubercle bacilli of the human type have been isolated from milk, and thus point out another source of danger from contamination by the tuberculous individual.

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TABLE.

DATA OF INOCULATION OF RABBITS WITH PURE CULTURES OF TUBERCLE BACILLI.

	Total Age of Culture	Generation	Age of Culture	Amount Inoculated	No. Rabbit	RESULT	GENERAL REMARKS
Culture I.	82 Days	3d	22 Days	0.5c.c.	320	Chloro-formed, 21 Days Ill	General Tuberculosis
Culture II.	95 Days	4th	20 Days	0.5c.c.	321	Died 18 Days	General Tuberculosis
Culture III.	76 Days	3d	25 Days	0.5c.c.	325	Died 16 Days	General Tuberculosis
Culture IV.	67 Days	3d	28 Days	0.4c.c.	326	Died 20 Days	General Tuberculosis
Culture V.	98 Days	4th	21 Days	0.5c.c.	327	Died 23 Days	General Tuberculosis
Culture VI.	79 Days	3d	30 Days	0.5c.c.	331	Chloro-formed, 17 Days Ill	General Tuberculosis
Culture VII.	69 Days	3d	26 Days	0 5c.c.	332	Died 15 Days	General Tuberculosis
Culture VIII.	63 Days	3d	21 Days	1 mg.	181	Killed 80 Days	Few Tubercles in Lungs and Kidneys
	42 Days	2d	21 Days	1 mg.	521	Alive 63 Days	Gained in Weight

A CASE OF EXTENSIVE PULMONARY THROMBOSIS COMPLICATING PNEUMONIA;
A CASE OF EXTENSIVE SINUS THROMBOSIS;
A CASE OF STENOSIS OF THE ISTHMUS OF THE AORTA IN AN INFANT.

E. A. PARK, M. D.

Dr. E. A. Park presented for Dr. John Howland a specimen comprising the left lung of a child, one and a half years old, who was admitted to the New York Foundling Hospital in a moribund condition, and died four days later. Clinically, the case was one of severe pneumonia complicated with empyema. At autopsy the left lung was found to be consolidated, except for a narrow strip along the anterior border of the upper lobe. The surface was grayish brown, and the lower half was covered by fibrino-purulent exudate. On section, the cut surface was a dirty gray color, but presented, in the upper lobe, irregular, dark red areas, from 0.5 to 2 cm. in diameter, which were poorly outlined, shading into the gray. The lung substance was unusually dry and friable. The vessels, except in the narrow strip along the anterior margin of the upper lobe, were everywhere thrombosed, those in the gray substance with fibrinous clots, those in the red areas with dark blue clots. The clots were not adherent to the vessel walls. The left pulmonary artery and veins were plugged with fibrinous clots, which projected from their mouths into the cavities of the pulmonary artery and left auricle, respectively.

Microscopical examination was merely confirmatory of the gross diagnosis. The pneumonia was fibrinous in the gray stage; but numerous areas of the lung were seen to be necrotic, with the lung structure no longer distinguishable. The red areas owed their color to the presence of red cells with large depositions of pigment in the alveoli and parenchyma. No inflammatory condition of the vessel wall was noted. There was a recent pneumonia of the lower lobe of the right lung. The kidneys

showed parenchymatous inflammation. The liver was fatty, the spleen hyperplastic.

No cause for the extensive thrombosis of the left lung was found outside of the lung itself.

Dr. Park also presented for Dr. Howland a specimen from a case of sinus thrombosis. The clinical history was, in substance, as follows:

The patient was a four-year-old girl; healthy; no antecedent history. She had had two attacks of pneumonia, both ushered in by severe vomiting and cerebral symptoms; signs of consolidation appearing late, and double otitis developing with the decline in temperature. The attacks were of about two weeks' duration, and occurred a month apart. Following the first, the patient suffered from pharyngeal diphtheria and had not regained her former weight and appearance when the second attack began. She showed indefinite nervous symptoms which suggested hysteria. About two days after the subsidence of the second attack of pneumonia, the right side of the face and the right hand and arm began to twitch. For one day these movements seemed to be under at least partial control, but on the second day they became involuntary and involved the entire right side. The temperature rose to 101 ; the mind remained clear. On the third day after their onset the twitchings had become constant on the right side, and at times appeared on the left side. The temperature rose to 102 . That night the child suddenly became sicker, sank into coma, and died on the following morning with a temperature of 105°.

There was free drainage from both ears and no evidence of mastoid disease. The white blood cell count was 30,000, polymorphonuclears 87 per cent. Spinal puncture showed an excess of clear fluid under pressure. There was no Kernig sign and no rigidity of the neck.

At autopsy there was found extensive thrombosis of the sinuses of the dura. The clots were larger on the right than on the left side, and on the right side extended into the jugular bulb and beyond it for about 4 cm. into the neck. The left bulb

was free. The superficial veins of the brain showed thrombosis and the pia adjacent showed extensive subpial hemorrhages. Whether there was cerebral softening; and, if so, what the extent and location of it was could not be determined (the body was five days old).

The right lung showed a resolving bronchopneumonia and adhesive pleurisy; the kidneys showed parenchymatous inflammation. The mastoid antra and the cavities of the middle ear contained pus, but their bony walls were sound. No extension from the right ear to the jugular bulb was demonstrated.

It is well worth noting that the sinus thrombosis apparently had originated, and was certainly more extensive on the right side of the brain, while the irritative symptoms appeared first, and remained most active on the right side of the body.

Dr. Park next presented a heart showing stenosis of the isthmus of the aorta, removed from an infant dying immediately after birth. The labor was long and difficult, and finally instrumental. The fetal heart sounds during the latter part of labor were especially loud and slow, about eighty to the minute. No murmur was heard. At birth the child was very white, and made no attempt to breathe. The heart action continued for fifteen minutes, growing feebler and slower until it ceased altogether.

The heart was larger than normal. The right ventricle was markedly hypertrophied, the musculature appearing like that of an hypertrophied left ventricle in an adult. The cavity was also larger than normal. The musculature of the left ventricle was, on the contrary, poorly developed, and the cavity was of normal size. At the point of origin of the subclavian from the aorta, the latter was narrowed to a diameter of 0.5 cm. The ductus arteriosus, opening into the aorta just distal to the stenosis, presented an orifice of about the same size as that of the aorta at the point of stenosis, but became larger as the opening into the pulmonary artery was approached. This opening was 1 cm. in diameter. The foramen ovale was closed. No other defects in the heart or body were found. The aorta proximal to the ste-

nosis, and the vessels given off from it, were normal. The brain was normal. The lungs were atelectatic, except for scattered areas of inflated lung due perhaps to attempts at insufflation by the obstetrician.

CASES OF FAILURE OF ROTATION OF THE GUT; A CASE OF CONGENITAL DIAPHRAGMATIC HERNIA.

GEORGE SMITH, M. D.

Dr. George Smith presented two specimens showing failure of rotation of the gut. The first was removed from an infant, one week old, who died of malnutrition; the second from a child, eight months old, who died of bronchopneumonia. Both cases were seen at the New York Foundling Hospital.

Upon opening the abdomen of the first child, the small intestine was found entirely on the right side. On lifting the intestine, a clear space was found with nothing but the kidney fixed. On the left side, the large intestine, the ascending and descending colon, the cecum, and the appendix appeared. The cecum and the appendix were in the left iliac fossa. The intestine itself was kinked, as was usual in these cases, especially in the duodenal portion where there were adhesions. The cecum was infantile and crescentic in form. The situation of the intestines showed that no stages of rotation had taken place.

In the second specimen was shown what was believed to be the primary mesentery and hind-gut, which were fixed directly in the mid-line. There was no fixation of the ascending colon on the right side. As the gut was thrown over to the right side, in the left fossa and by the pelvic brim there was found the cecum with the appendix. The sigmoid and descending colon were attached to the mid-line. This was thought to be the original mesentery of the hind-gut. In other words, this

gut did not swing to the left and become fixed as is normal, so as to form the subsigmoid fossa. Nothing else abnormal was found in either case.

Dr. Smith also presented a specimen of congenital diaphragmatic hernia. The child was born with the aid of forceps and was very slightly asphyxiated at birth. Six hours after, it became cyanotic and died. Upon opening the abdomen only the descending colon, two kidneys, and the liver were found. Upon close inspection, however, the head of the pancreas was discovered. There was also a deficiency in the left side of the diaphragm itself, due to an arrest in development; and through this rent in the diaphragm most of the intestines had passed into the left pleural cavity. The left lung was rudimentary. The progress of the intestine was rather peculiar. The esophagus was traced in the posterior mediastinum. It passed first under the diaphragm and then up through the hernial opening into the stomach. The stomach ran anteriorly in the pleural cavity; but the duodenum passed into the abdomen to receive the bile duct. The duodenum again entered the thorax by the hernial opening, so that the duodenal-jejunal junction lay in the pleural cavity. The remainder of the intestine, with the exception of the descending colon, was in the thorax. The opening in the diaphragm admitted two fingers. The presence of the intestine had prevented the growth of the left lung. The heart was pushed to the right side, but was normal. The right lung was perfectly normal. The patient had been examined at the time of the dyspnea, and the heart sounds were heard to the right of the sternum. There was marked dulness and no breath sounds over the entire left side of the chest. Over the right side the breath sounds were normal.

EXPERIMENTAL GLOMERULAR LESIONS DUE TO VENOM.

RICHARD M. PEARCE, M. D.

Dr. Richard M. Pearce presented two slides under the microscope to demonstrate the lesions in the kidney due to the venom of the rattlesnake (Crotalus adamanteus). During the last few months he had been interested in the experimental production of edema and had used venom as a vascular poison. The venom of the rattlesnake contains a body to which Flexner and Noguchi gave the name "hemorrhagin" and which, by injury to the endothelium of blood vessels, causes hemorrhages. In experiments which were conducted on rabbits it was possible so to grade the dose that the injury led to exudation of serum without hemorrhage. He found that there occurred an injury of the endothelial lining of the tuft of the glomerulus allowing exudation and constituting an interesting form of vascular nephritis. One slide showed a pure form of the lesion with fluid exudate; the other showed the venom lesion with hemorrhages into the glomerular tuft and necrosis of tubules due to simultaneous administration of potassium chromate.

Discussion.

Dr. Jas. Ewing said that it was a remarkable thing to find an agent picking out the endothelial cells alone for injury, and he wished to ask Dr. Pearce if he found that these were the only cells of the kidneys that were injured.

Dr. Pearce said that with the venom was administered a chrome salt and large quantities of water by the stomach, the idea being to show the relative importance of vascular and renal injury and plethoric hyperemia in the production of edema. A widespread edema was obtained with an accumulation of fluid in the pleural and peritoneal cavities. The venom not only injured the vessels, but had also neurotoxic, hemolytic and hemagglutinative properties. Because of the evidences of general ede-

ma and the appearance of small hemorrhages in the liver, mus-
cles and serous membranes, the endotheliotoxic action of the
venom was considered to be universal and not limited to the
glomeruli. The glomerular lesion was but one manifestation of
the action of the venom, but interesting on account of its pe-
culiar character and its resemblance to certain forms of toxic
glomerulo-nephritis in man.

A CASE OF APLASTIC ANEMIA.

LUDWIG KAST, M. D.

Under normal conditions the human organism replaces the
loss of blood by the formation of new blood cells. If we ex-
amine the red cells, we find, in the different forms of anemia,
cells in the circulating blood which indicate that a new forma-
tion is going on in the bone marrow. There is as yet not a
complete accordance of opinion as to what may be considered
signs of regeneration in the circulating blood; but the appear-
ance of nucleated reds in the circulating blood is undoubtedly
a sign of regeneration. Thus in all severe anemias we find
erythroblasts in the circulating blood, and the bone marrow in
a state of increased erythrogenic function; nucleated red cells
are far more numerous than under normal conditions, and
wherever there is red lymphoid tissue, as in the ribs, vertebrae,
and epiphyses of the long bones, we find these cells generally in
indirect, sometimes in direct, multiplication. The shafts of the
long bones, however, do not contain any lymphoid tissue; they
show only fat. In severe anemias or in those of long duration
the process of regeneration seems to be so intense that the fat
in the diaphyses is replaced by new tissue, red in appearance, and
capable of producing erythroblasts and erythrocytes. In some
cases also the spleen and other organs show new erythrogenic
centers. Now the outcome of an anemic condition, of course

not considering complications, depends upon whether the supply equals the demand. If this is the case, the individual gets well, temporarily or permanently. If the balance between destruction of red cells and regeneration of red cells is such that there is always more loss of red cells than reproduction, the individual will finally succumb, in spite of the regenerative efforts of the hematogenic tissues.

In another group of cases the patient succumbs to a rapidly developing and persisting anemic condition without any signs of regeneration in the circulating blood. Either the bone marrow shows no reaction whatever, and in such cases it appears as if the individual must have bled to death in such a short time that there was no chance for regeneration; or the bone marrow shows fatty degeneration in places where normally it appears red.

It is, therefore, quite reasonable to divide the anemias roughly into two groups: anemias with erythro-regeneration, and anemias without erythro-regeneration, into sthenic or asthenic anemias. Ehrlich has called the latter form of anemia, "aplastic," and this term has been generally accepted. From the standpoint of the pathologist, the term aplastic does not seem to be correct, because this is not an inborn quality of the bone marrow. It is perhaps better to use the term "myelophthisic anemia" (Pappenheim).

I wish now to report such a case of asthenic or myelophthisic anemia which I observed several years ago in the clinic of Prof. Pribram of Prague, Austria.

The patient was a woman, aged twenty-five years, without any noteworthy points regarding heredity or diseases previous to her fatal illness. Bleeding began from the gums and the nose. Upon entering the hospital the patient showed all the typical subjective and objective signs of a severe anemia, very little loss of weight, retinal hemorrhages. During our observation of ten days she began to menstruate with profuse flow. Her temperature was between normal and 103; she vomited frequently. It was impossible to stop the bleeding from

the uterus or from the gums. The blood was examined every other day and showed: erythrocytes between 800,000 and 400,-000; leucocytes between 1,900 and 2,000; hemoglobin from 20 to 10 per cent. (Fleischl-Miescher). Morphologically in smears, I found poikilocytosis, many microcytes, very few poly-chromatophilic erythrocytes, only one or two normoblasts on one slide. Of the leucocytes, 60 per cent. were small lympho-cytes, 5 per cent. large mononuclears, very few eosinophiles; no myelocytes.

The complete post-mortem examination was performed by Prof. Chiari. Aside from an intense anemia and fatty degen-eration of the organs, I wish to mention only the following note-worthy pathological changes: Hemorrhages in the pericardium; brown pigmentation of the liver; the uterus in a state of men-struation; a hemorrhage in a small cyst of one ovary; macro-scopically the bone marrow of the sternum and of one rib pale red; the bone marrow of the right femur mostly fatty and yel-low, with lipomatous lymphatic spots of very pale color. The liver showed, upon addition of ammonium sulphide, a marked green color as a sign of hemosiderosis. I examined also the marrow of several ribs, of the sternum, and of the right femur, the spleen, and a bronchial, a mesenteric, and a retroperitoneal gland. I was fortunate enough to obtain one rib two hours post-mortem, which was, of course, very valuable for the mi-croscopical examination. Without entering into details of the microscopic examination of the hematopoietic organs, I wish to state that only in spots could lymphoid tissue be found, the re-mainder was either entirely fatty or fat mixed with debris of red and white cells. The spots of lymphoid tissue, however, showed, aside from the white cells, an increased amount of nu-cleated reds, mostly normoblasts, but also megaloblasts, many in the state of division. It appears from the microscopical study of the bone marrow that in most places a fatty degeneration took place, while at the same time in some spots an active re-generative action was taking place. The details of the clinical and pathological findings will be published elsewhere.

Discussion.

Dr. JAMES EWING said that he had the impression that in the anemias a relative deficiency of the red bone marrow was rather common. He had been led to believe that in the aplastic anemias the symptoms were not wholly due to the lack of blood-forming marrow, but rather that the absence of red marrow gave the anemias certain clinical features. One should look for other factors as further causes of the anemia. With regard to the fatty change, he said that this was not a true fatty degeneration, but a fat invasion of the lymphoid tissue and bone marrow.

Dr. HARLOW BROOKS asked if the change in the bone marrow was not somewhat like the fatty replacement seen in the bone marrow in the anemias of senility.

Dr. KAST said that he thought Dr. Ewing was perfectly right in assuming that the greater part of the fat was a replacement. It was not a degeneration in the histological sense of the word, but in the functional sense. There was some fatty degeneration of blood cells, but mainly a replacement of lymphoid tissue by a fatty tissue had taken place. Undoubtedly it would in time be shown that different individuals reacted to the hemorrhages, or to the hemorrhagic process, in different ways. Undoubtedly in debilitated individuals and in old individuals without much resistance, there would sooner appear such a set of symptoms as in "aplastic anemia," and the result would be the replacement of lymphoid tissue by fat. As a matter of fact, Pappenheim, during the past year, used this point to prove that all anemias were secondary.

Proceedings

of the

New York Pathological Society.

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Dr. Horst Oertel, *President.*

THYROID TISSUE IN OVARIAN EMBRYOMATA.*

F. C. WOOD, M.D.

Dr. F. C. Wood presented a series of specimens. He said
that recently a great deal of interest had centered in the pres-
ence of thyroid tissue in ovarian embryomata. He used the
term embryomata advisedly, because it seemed very difficult
to make an accurate separation between a dermoid and a tera-
toma of the ovary. It was, therefore, better to call the tumors
he was about to show, ovarian embryomata and so avoid dis-
cussion.

Specimen 1. This was an ovarian cyst which was removed
from a woman in good health She had no enlargement of the

thyroid. The cyst was filled with a reddish fluid, and was at first supposed to be an ordinary ovarian cyst. The remnants of the ovary on one side of the cyst were examined and sectioned, and were found to be composed almost entirely of thyroid tissue. The only other tissue besides the connective and thyroid tissue were fragments of bone with Haversian canals. There were no hairs present. This was one of the simplest types of cyst.

Specimen 2. This specimen had been largely cut up for examination, and was originally only a small cyst. No hairs or teeth were found; only connective tissue and thyroid tissue.

Specimen 3. This was a more complicated specimen than either of the previous ones shown. The patient was forty years old, and some time ago had had her breast removed. Although it was impossible to verify the diagnosis, it was assumed that she had had a carcinoma of the breast. Two years after the operation, she entered St. Luke's Hospital complaining of pain in the pelvis, in the coccyx, and in the lumbar region. It was supposed that she was suffering from a recurrence of the carcinoma, and an exploratory laparotomy was done, and a double cyst of the ovary found. There was a parovarian cyst which had collapsed. There was a small but normal tube. The ovary had practically changed into a multilocular growth. All the solid portions of the ovary were composed of thyroid tissue. There were no hairs in the cyst, which was lined with flattened epithelium. There was apparently no formation of bone or teeth. Curiously enough, the thyroid tissue showed the development of carcinoma. The question arose whether this was a metastasis of the breast carcinoma developing in the ovary. There were in the carcinomatous tissue, however, areas like the secreting portions of the thyroid, i. e., colloid tissue. This looked like what one saw in true carcinoma of the thyroid. It seemed to Dr. Wood, therefore, that this was a primary carcinoma developing in thyroid tissue. The patient had had no recurrence from the original carcinoma of the breast, and she was still in good health. Evidently the ovarian

tumor was the cause of the pain in the pelvic region.

Specimen 4. This was a case of interest from the start. The patient was a woman in the German Hospital, who had two ovarian cysts which were very large and contained an enormous amount of hair and sebaceous matter. They were multilocular and contained a number of bony particles and teeth inserted at one point on the wall. There was also a mass of tissue present which could not be distinguished from ordinary thyroid tissue. There had been a sufficient quantity of this material to work on, and by making a chloroform extract it was shown that iodine was present; i. e., the thyroid tissue contained iodine, as did the normal thyroid.

There had been quite a dispute concerning the nature of the tumors, and some observers had considered them folliculo-mata and as not consisting of true thyroid tissue, but this view had now been given up. These cases were not very infrequent, and a number had been reported in which the thyroid tissue had been formed in ovarian tumors. Pick had stated that he had found thyroid tissue in seven out of twenty-one dermoid cysts. It seemed to Dr. Wood that Dr. Pick must have been lucky, for in his own collection he had never been able to find thyroid tissue, and he had examined more than twenty-one.

The history of these growths showed that they were, as a rule, benign in character, and did not tend to recurrences or malignancy. Probably these tissue remnants were of the same types as the cartilage, trachea, salivary glands, brain cells, etc., which were so frequently found in examining dermoid cysts of the ovary.

Discussion.

DR. ROBERT T. FRANK said he believed that Dr. Wood's collection of specimens covered the entire ground. A finer collection of specimens of teratomata, or teratomatous growths of this group, could not be found. The specimen of the greatest interest was the one in which carcinoma and colloid goiter were

found together. It was to be regretted that the primary carcinoma removed at the time of the excision of the breast could not be found. Because of this, nothing definite could be said as to whether there was a metastasis of the carcinoma in the teratoma, which would be extremely unlikely, or whether it was a carcinoma arising from the teratomatous growth. He thought the study of the clinical course might help. Teratomatous tumors containing goiter take a more favorable clinical course than do those, for instance, in which metastases of carcinoma localize in the ovary. Clinically these cases were of great interest, because in almost one-half the cases ascites occurs, giving a most malignant appearance. In spite of this, he had been able to collect from the literature but one case which showed a recurrence. Recently he had examined a similar case of teratoma, which consisted of three elements: 1. Bone to which was attached a molar tooth. 2. A corpus luteum. 3. The rest of the tumor was composed of thyroid tissue containing colloid material.

AN UNUSUAL CASE OF LYMPHATIC LEUKEMIA.

MARTIN REHLING, M.D., AND F. C. WOOD, M.D.

Dr. Martin Rehling presented the clinical history of a patient who was the sister of a physician, thirty-two years of age, with a negative family history; married for twelve years; one child nine years old; no miscarriages. The patient had become increasingly pale for one and a half years, felt tired; did not complain of pain nor seem to lose weight; no vertigo nor ear symptoms, but considerable headache for the past nine months; dyspnea and palpitation of the heart for about two months. For the last five months she had had bleeding from her gums, losing a few teaspoonfuls of blood. She had slept poorly for the last few months. Menstruation had ceased for some time, be-

ginning again three months ago. She had occasional rises of
temperature to 102° F.

The patient was a very pale woman, weighing 124 pounds.
There were numerous petechiæ all over the body. There was
slight fetor, but the mucous membrane of the mouth was not
gangrenous. The tonsils were normal in appearance. A few
glands the size of a pea were to be felt in the neck and groin.
The heart was not increased in size; the pulse rate was 122 per
minute; and a hemic murmur was to be heard at the base and
apex. The liver dulness reached to about one finger's breadth
below the costal margin. Some ascites was present, as was
also a moderate amount of edema of the extremities. The pel-
vic organs were normal. The spleen was about 22 cm. in its
longest diameter; it was hard and smooth to the touch.

In accordance with the blood examination made by Dr.
E. E. Smith on July 17, 1908, the diagnosis of lymphatic leu-
kemia was made, and treatment with arsenic and the Röntgen
rays was advised.

Nothing further was heard from the patient until the fol-
lowing December, when the report of the blood examination
made by Dr. F. E. Sondern and dated December 24, 1908, was
brought. In the meantime, the patient had been given sodium
cacodylate, but the Röntgen rays had not been used. Several
prominent consultants were seen, some of whom diagnosed the
case as lymphatic leukemia, others as splenic anemia or Banti's
disease. A blood report was also received from Dr. Goldhorn,
dated December 21, 1908, in which he diagnosed the case as
Banti's disease.

The patient finally entered the German Hospital and was
subjected to the Röntgen rays the following day, but the de-
pression and bleeding from the gums following the treatment
discouraged the patient's relatives, and another consultation was
held. The consultant was decided in his opinion that this was
a case of Banti's disease, and a splenectomy was decided upon.

On January 6, 1909, direct transfusion was done, and on
January 11, the splenectomy was performed. This was accom-

plished with but little loss of blood, and a blood examination made after the operation while the patient was still on the table showed practically the same conditions as existed before the operation.   The patient at first did very well, but later went into collapse, and death resulted on January 13, 1909.

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Dr. F. C. Wood said that he had examined specimens of this blood before the patient died; and, while it was rather unusual, he did not see how a diagnosis of splenic anemia or Banti's disease could be made from it.   The autopsy showed the body of a slenderly built woman with extreme anemia of the skin.   There was a rash over the lower extremities.   There were a few ecchymoses on the outer surface of the thighs.   A careful search was made for lymph nodes, but only a few small ones were found in the groins and the axilla.   On opening the abdomen, the intestines were found to be distended, and 100 c.c. of a thin bloody fluid was obtained from the peritoneum. General inspection of the abdomen revealed nothing in particular.   There were a few areas of fat necrosis in the omentum. The retroperitoneal lymph nodes were slightly enlarged, but not more than is often seen in other diseases.   The liver was very soft and a pale yellow, and looked anemic.   There was no evidence of leukemic infiltration in the kidneys.   The heart was practically normal. One of the lungs showed a few hemorrhagic areas which proved to be infarcts.   The intestines and stomach showed occasional petechial hemorrhages.   There were no other important lesions found except in the bone marrow, which was yellow with a few reddish spots scattered about.   In no place was there a diffuse hyperplasia of the marrow.   The spleen was soft, with a wrinkled capsule.   There were two or three rather large accessory spleens.   When fresh the splenic surface was dull red, almost a chocolate color.   It was soft, and did not look like a Banti's spleen.   There was practically no increase in the connective tissue.

Patient: Mrs. R. B.	Dr. E. E. Smith July 17, 1908	Dr F. E. Sondern Dec. 14, 1908
Hemoglobin	43% (Fleischl)	24%
Red Cells	2,060,000	1,000,000
	Size, small, moderate variations in shape; no microcytes. Fibrin formation not increased	Corpuscles generally large and somewhat varied in shape. Some poikilocytes; few microcytes. No nucleated reds found.
White cells	26,880	27,800
	Polynuclears ..... 4.6% Lymphocytes..... 82. Large mononuclears and transitionals .... 13. Eosinophiles...... 0.4 Mast cells .... 0.	Polynuclears ..... 5.2% Large lymphocytes 7 4 Small " 87.4 Other forms ...... 0.
Index	1 (ratio of reds to whites 1:77)	1.2
	No malaria plasmodia. *Diag.:* Marked anemia with proportional decrease in hemoglobin and erythrocytes. Large absolute and relative lymphocytosis. These are the findings of *Lymphatic Leukemia.*	No malaria plasmodia. *Note:* Marked diminution in the amount of coloring matter and in the number of red corpuscles with a leucocytosis as stated and a marked relative lymphocytosis limited to the small type. The anemia is extreme and while the increase in leucocytes is unusually slight, it, together with the differential count would indicate a *Lymphatic Leukemia,* not a splenic anemia.

	Before Transfusion	*After Transfusion*
Dr. Goldhorn Dec. 21, 1908	Dr. D. Jan. 6, 1909	Dr. D. Jan. 9, 1909
19% (Sahli)	15% (Fleischl)	30%
1,100,000	850,000	2,240,000
Some microcytes and poikilocytes; few washed-out corpuscles; resistance of cells poor; some polychromatophilia. No nucleated reds.		Some anisocytosis. No nucleated reds.
22,500	11,200	8,100
Polynuclears ..... 5.5% Large lymphocytes 11.5 Small " 78.5 Transitionals ...... 4.	Polynuclears ...... 3.% Lymphocytes...... 94. Large mononuclears 3. The polynuclears are very small, about the same size as the small lymphocytes.	Polynuclears ...... 2.% Lymphocytes...... 95. Large mononuclears 3. Polynuclears are the same size as small lymphocytes.

0.9 (minus)

Total polymorphonuclears 1,230. as against a normal average of 4,000.
Blood pressure 130.
Not a Leukemia.
Considering the blood and urinary findings in conjunction with the clinical course, I regard this as a case of Banti's disease.

Before Splenectomy Dr. D. Jan. 11, 1909	(On operating table) After Splenectomy Dr. D. Jan. 11, 1909	Day of Death Dr. D. Jan. 13, 1909
28%	28%	23%
2,150,000	2,090,000	2,025,000
Poikilocytosis; anisocytosis No nucleated reds.	Poikilocytosis; anisocytosis. No nucleated reds.	Poikilocytosis; anisocytosis. No nucleated reds.

8,100	16,000	18,000
Polynuclears .... 3. % Lymphocytes..... 94. Large mononu.... 2. Eosinophiles...... 0.5 Basophiles 0.5	Polynuclears ..... 3. % Lymphocytes..... 94. Large mononu.... 2. Eosinophiles ..... 0.5 Basophiles........ 0.5	Polynuclears ...... 3. % Lymphocytes...... 93. Large mononu..... 3. Eosinophiles ...... 1. Basophiles......... 0.

A great many sections were made of the spleen and of the lymph nodes found, and particularly from the liver. The spleen was lymphoid, had lost its normal architecture, and was largely made up of lymphocytes. There was no increase of fibrous connective tissue. It looked like a leukemic spleen. A point of interest was in the capsule, which was covered with a layer of lymphocytes, four or five cells deep in some places and deeper in others where the whole tissue was infiltrated with lymphocytes. The splenic sinuses showed an infiltration of lymphocytes under the endothelium. There were a large number of plasma cells among the lymphocytes in the spleen pulp.

The lymph nodes were rather atrophic and contained very few lymphocytes. They were edematous, with large sinuses, the latter containing many phagocytes. All were of the same type, though some were rather large. There was a lymphoid infiltration of fat about the lymph nodes. The liver showed parenchymatous changes and an infiltration with lymphocytes in Glisson's capsule. The kidneys also showed a parenchymatous change.

The picture was very puzzling, and it was difficult to classify the case. It might be thought to be an aplastic anemia, but the large spleen was against that, as was also the high lymphocytosis.

What seemed to fit the case better was the diagnosis of lymphatic leukemia. Dr. Wood had seen a similar case at St. Luke's, in which the same lesions were found in the spleen, with an immense hyperplasia of the bone marrow, which was diagnosed as acute lymphatic leukemia, although the leucocytes did not run high. The probable diagnosis here, then, is lymphatic leukemia with the chief overgrowth in the spleen itself, and rather extensive involvement of the marrow. There is no hyperplasia of the bone marrow, and no hyperplasia in the nodes.

Dr. Wood said that he had not been able to find any cases in the literature which were exactly similar. Several had been reported in which the chief lesion was in the spleen, but they

were not just like this case, which was very interesting for study and discussion.

Discussion.

Dr. Richard M. Pearce said that too much stress should not be laid upon the accumulation of lymphoid cells beneath the endothelium of the splenic sinuses. This he had sometimes seen in scarlet fever, in bubonic plague, and in other infectious diseases. It was a very interesting condition, but one which occurred now and then without being peculiar to the disease with which it appeared to be associated.

Dr. Wood replied that he was aware that lymphoid infiltration was seen in some infections, but in going over a large series of spleens he had not found such lesions in non-infected cases, and under the circumstances it seemed rather interesting that he should have two recent specimens—one an undoubted lymphatic leukemia, and this one—both showing the same lesions.

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A CASE OF STOKES-ADAMS' DISEASE.

L. F. BISHOP, M.D., AND J. H. LARKIN, M.D.

Dr. L. F. Bishop presented the clinical history of a case of Stokes-Adams' disease which he described as the most typical and classical one he had ever seen or read of.

The patient, T. M., was admitted to the Lincoln Hospital on October 13, 1908, and died October 22, 1908. His family history was negative. He had previously had no important illness except measles, whooping-cough, and smallpox when a child. Later he had had muscular rheumatism, and twenty-five years ago had had a sunstroke; but he had always

been considered a healthy, strong, hard-working Irishman. He drank whiskey moderately. There was no history of syphilis.

On October 12, while in bed, he felt as though he were whirled around, and had a great buzzing in his ears, especially the right one, in which he had been gradually growing deaf. After that he had three similar attacks, and came to the hospital complaining chiefly of these attacks and of feeling weak. He said that the attacks and vertigo came on without premonition, and that between the attacks he felt perfectly well, excepting that he was weak.

On admission, he appeared to be a fairly well-developed but poorly nourished man. The pupils reacted to light and accommodation. The tongue was coated; the lungs were negative; the heart was in the median line; there was no murmur. The heart beats registered thirty-six per minute; the beats in the neck three to one at the apex. The abdomen was negative. The extremities showed nothing. It was a very brief and negative history, and the findings in the case were chiefly objective.

Photographs showed the patient sitting up in bed, and again shortly after one of these attacks, and depicted the attitude and expression of extreme exhaustion and depression. The jugular tracings were also presented, showing the much more rapid pulsations in the vein and the extremely slow apex beat.

The case was a typical one, and the diagnosis was made by the Junior half an hour after the patient was admitted to the hospital. There was no doubt about the diagnosis.

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DR. J. H. LARKIN said that there was little to say about this curious case of Stokes-Adams' disease. He had seen a number of these cases and had been trying to collect them in such a way as to make definite microscopical examinations of the various conditions found. This particular heart lesion seemed to be of the calcareous type. In the aortic vestibule there was diffuse thickening of the endocardium, a retraction and thickening of the mitral valve, and diffuse calcification in

the region of the bundle of His; otherwise the heart showed little change. The cavity was only moderately dilated; there was a normal amount of musculature, and a slight amount of atheroma in the aorta. The lesion in this heart appeared to be in the typical place in the vestibule.

Outside of the microscopical condition there was nothing of particular interest, the main interest centering in the clinical history.

The case was one of the most marked types seen at autopsy. It seemed probable that the hearts were not examined in the course of ordinary autopsies as completely as they should be. For the past few years Dr. Larkin had been systematically collecting hearts, for the purpose of making a thorough and systematic study, and he had now between 150 and 180 hearts which he intended to examine without knowing anything about the history.

It did not seem probable that the microscopic examination of these calcified hearts would yield very much information. In other hearts where there were tumor and sclerosis of the aortic valves, and where there were gummatous infiltrations, one was more likely to get correct information in regard to the bundle of His. In the sheep heart, the bundle of His could be dissected out, but this was impossible in the human heart. Dr. Larkin had a number of sheep hearts which had been examined microscopically, and thought there was a great discrepancy of opinion as to the nature of this bundle, whether it is a pure muscular or a nerve bundle. He was inclined to throw over the idea that it is a muscle bundle. He had put a number of normal and abnormal hearts through the Cajal method of staining, and felt that he had demonstrated certain points in regard to the bundle, topographically and microscopically. It was at least mixed with nerves, if not entirely composed of nerve fiber, and at present he was more inclined to view this condition as one allied to a nerve lesion in the so-called bundle of His.

Further microscopic work must be done on many hearts in regard to the lesions which we find so prominent in and

around the aortic vestibule, and it would be well for those working along this line to study them carefully to obtain more knowledge regarding the cardiac nerve fibers and the so-called bundle of His, as to whether it is a nerve bundle or a muscular structure.

ON THE TYPE OF CULTURES FROM OLD CUTANE-
OUS TUBERCLES OF BUTCHERS.

ALFRED F. HESS, M.D.

(From the Research Laboratory, Department of Health, New York.)

It is now generally conceded that the tubercle bacillus of cattle at times incites tuberculosis in man. This conclusion has been definitely established only through the possibility of distinguishing between a bovine and a human type of bacillus, and through employing this method and isolating the bovine type of organism from human tuberculous infections. The studies thus far carried out in different countries, using the same methods of differentiation, agree in charging the human bacillus with a marked preponderance of infections. In this connection, however, there is one disturbing criticism that is now and again brought forth to shake the confidence imposed in these conclusions, based as they are on the differentiation of the types of bacilli. It is claimed by some capable workers that it is possible for the bovine bacillus to be so altered by years of sojourn in the human tissues that its essential characteristics become altered and it simulates the human type of bacillus. Without doubt, if this metamorphosis can readily take place, some of those infections which we now believe to have been of human origin may well have had their source in bovine infections of years ago, and it is to no purpose to designate them as human. In fact, if this were so, the entire method of differentiation which

has accomplished so much in the past decade, and promises so
much more in the practical and theoretical study of tuberculosis,
would have to be regarded as not only unreliable, but misleading.

The main difficulty in studying this question in man is that
we are rarely certain of the nature of the original infection,
and accordingly cannot judge of the change of type. Our main
reliance is generally circumstantial evidence. An exception to
this rule, however, is furnished by those few cases of inoculation
tuberculosis where the bovine source of infection is definitely
known. I have with difficulty found two cases of this nature,
both in slaughter-house workers, and report a study of them,
coupled with some other experiments relating to the stability of
the types of tubercle bacilli.

Case 1. This man had been employed in his present trade
for seven years. Four years ago, while slaughtering an animal,
he cut the middle finger of his right hand on the pointed end
of a rib. He gave no thought to this injury until he found that
it was slow to heal; he then merely applied various ointments.
Gradually a nodule appeared at the site of the wound which as-
sumed its present condition. He was aware of the tuberculous
nature of this nodule, and in fact directed me to another worker
who had the same skin lesion. I shall not enter into a minute
description of the appearance of this nodule. It was the size
of a large pea, brownish red and very firm in consistency. The
glands at the elbow and axilla were not enlarged. The general
health of the man was excellent.

Case 2. This case was very similar to the previous one.
This man, while slaughtering a tuberculous cow, cut himself
with a knife across the knuckles. This accident happened about
six years ago. He remembered the date, as he was forced by
this disability to quit work for some weeks and to enter the
employment of another firm. As in the previous instance, a
nodule appeared at the site of injury. The nodule was situ-
ated over the fourth left metacarpal joint, and resembled the
tubercle described in the previous case, excepting that its sur-
face was rougher and papilliform. This man also was healthy

to all appearances; however, a large hard epitrochlear gland was palpable at the right elbow.

Both of these men were induced to have these nodules excised. After excision the surface of the growths was removed, and they were thoroughly washed in sterile water. Two guinea-pigs were inoculated subcutaneously with each growth. All four animals developed tuberculosis. It is not necessary for me to give in detail the method of isolating tubercle bacilli from the tissues or the criteria for differentiating the types. The method employed was that now generally followed and made use of by me in previous studies. The cultural growth from these two cases proved to be very similar; in fact I could not distinguish between them. They both grew sparsely on egg media. They also showed a high degree of virulence for rabbits, producing a generalized tuberculosis when inoculated intravenously in the dose of one milligram. In other words, they were typically bovine.

Before discussing these results I shall describe an experiment undertaken with the object of transforming the bovine type of the tubercle bacillus into the human type. An attempt was made to produce a culture medium resembling in its composition as closely as possible the human tissues. From the outset the inherent variance between an artificial culture medium and the living tissues was clearly realized. For this purpose, however, what may be termed a "human-placenta glycerin broth" was devised. Human placenta was obtained under strict aseptic precautions and from this a broth was made, treating the placenta just as the beef is treated in preparing the broth for common use. One per cent. peptone, one-half per cent. salt, and five per cent. glycerin were added. The entire preparation of this culture medium was conducted with all possible aseptic precautions. In order not to destroy the complement of the human placenta, heat was applied only to 55 C. It was possible, in most instances, to obtain a sterile broth by means of filtration through a Berkefeld filter.

Two bovine strains of known virulence, one of them hav-

ing been under artificial cultivation for many years, the other only recently isolated, were grown upon this culture medium for nine months, comprising eight generations. At the end of this period their virulence for rabbits was found to be as marked as at the beginning, showing that in this respect they had not approached the human type. In fact the only change that was noted was one to be anticipated from artificial cultivation of any nature, namely, a greater facility of growth in the case of the strain which had been the more recently isolated. As this experiment was very laborious, and promised so little, it was discontinued.

The question of the stability or variability of the types of tubercle bacilli has been discussed so frequently that I shall not review the testimony. However, in connection with this report, a few words upon this subject seem in place. From the outset it should be realized that this question has a practical as well as a theoretical aspect, and that the two need not be in absolute accord. The former considers whether it is in any way possible, by natural or artificial means, to convert one type of bacillus into another type; the latter whether the bacilli isolated from man and designated as human have been converted in his tissues from an original bovine type. These two viewpoints must not be confused. It is true it has been demonstrated that under artificial cultivation strains may be greatly changed in their cultural and biological characteristics. Indeed, a culture isolated almost ten years ago from a cow, and kindly sent to me by Prof. Leonard Pearson, I recently found to simulate the human type both in luxuriance of growth and diminished virulence for rabbits. However, even after this long period of artificial cultivation, its virulence was still greater than that of cultures of the human type. Another bovine culture of about the same age was found to be markedly virulent for rabbits. However, such experiments clearly cannot be translated into practical evidence on this question. Again, it may be advanced that experiments have been reported showing a conversion of human into bovine bacilli by means of passage through cattle or of bovine into avian ba-

cilli by means of passage through birds. However, even if we accept these interpretations, and forego the criticism that has been levelled at them justly by others, we find these experiments to be very few in number and far outweighed by the many others where no conversion of type was effected. When we consider the practical side of this question and draw our arguments from what we know of tubercle bacilli in man, the following should be borne in mind: It is true, atypical types have been isolated by many investigators, strains neither typically human nor bovine. This intermediate group may, in part, be accounted for by attributing the variation to a change of environment, for example, of bovine bacilli in the new environment of human tissue. These atypical strains, it should be remembered, are exceptional: among three bovine and four human strains which I have isolated from man none belong to this category. Furthermore, this deviation from type cannot be regarded as evidence of the possibility of a complete change of type. In this connection it is worthy of note that typical bovine bacilli have been isolated from calcareous lymph nodes of human beings; in such instances the bovine bacilli must have existed in the human tissues for years without undergoing transformation. It has never been shown that the older the tuberculous lesion the less the likelihood of isolating bovine bacilli from man; and yet this corollary should obtain if the bacilli are readily converted in the human tissues. The question may be approached from another point of view. It is well known that no case of primary pulmonary tuberculosis has been indisputably proved to have been incited by the bovine bacillus. These cases form the great mass of tuberculosis and have been studied more than all others. If this form of the disease is due, in some instances, to a bovine bacillus which has been transformed in the human body, we should at least occasionally meet with this type of the bacillus in the early stage of the disease before it has been converted into the human type. Not only do we know that this is not the case, but we find that even the intermediate types are rarely met with in the primary pulmonary cases. So that it would seem

from a practical standpoint the question of transmutation of types may well be disregarded, and we can safely continue to investigate the etiology of tuberculosis by means of differentiating the types of bacilli.

The two cases of cutaneous tuberculosis which I report claim some degree of interest because they constitute bovine infections occurring in adults. The fact that they remained localized should not be attributed to the low degree of virulence for man of the bovine bacillus, as it is well known that cutaneous affections due to the human type of bacillus, such as lupus or the "anatomical tubercles" contracted in the dissecting room, likewise do not tend to systematic invasion. Their main significance, however, lies in the fact that they furnish exceptional instances of bovine tubercle bacilli which have lived in the human tissues for many years without acquiring characteristics of the human type. From this point of view they constitute evidence against the conversion in the human tissues of bovine bacilli into human tubercle bacilli. It would be interesting and of undoubted value if those who have access to similar long-standing cases of tuberculosis would make them the basis of a bacteriological study.

A MEDIASTINAL TUMOR WITH INVOLVEMENT OF THE LUNG, PERICARDIUM, AND HEART: SYPHILIS OF THE LUNG.*

LINDSAY S. MILNE, M.D.

The specimen of a mediastinal tumor was obtained at the autopsy on an Italian, thirty-six years of age, who had originally come under observation for pain in the upper part of the front of the chest and cough. The commencement of his illness had

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* To be described in detail in the Publications of the Russell Sage Institute.

dated back three months and had been associated with a progressively developing edema of the right side of the face and neck, the right upper extremity, the right side of the chest and abdomen, and the scrotum and penis. During the last two weeks of his illness he had complained of some dysphagia for solid foods, and had also suffered from severe spasms of tracheal coughing.

On physical examination, it was found that the veins on the front of the chest, particularly on the right side, were very much distended. The heart was extensively displaced downward and to the left, and it was of interest to note, considering the condition of the heart disclosed at autopsy, that there were no audible cardiac murmurs. The entire right side of the chest was absolutely dull on percussion, due to some extent to large quantities of slightly blood stained serous fluid which, from time to time, were removed from the pleural cavity. Over the front of the sternum, down to the level of the fifth rib and to some distance on either side, there could be heard loud conducted tracheal breathing, but no heart sounds. The lower border of the liver apparently extended down two inches below the costal margin in the right nipple line.

The blood, besides showing a moderate degree of anemia of a secondary type, contained an average of 10,000 leucocytes per c. mm.; polymorphonuclears, 83.2 per cent.; lymphocytes, 13 per cent.; large mononuclears, 2 per cent.

In the course of his illness emaciation was extremely rapid and the edema rapidly increased, spreading slightly to the legs and to the left side of the body before death occurred.

The autopsy showed that the diaphragm was practically flat with the lower costal margin, and that the liver, in consequence, had been displaced downwards. Both pleural cavities, but especially the right, contained a large amount of slightly blood stained fluid. The mediastinum was largely occupied by a large, oval, coarsely nodular tumor mass which extended upward one and one-half inches above the level of the episternal notch and downward to the level of the junction of the fifth rib with the

sternum. Laterally, it extended two-thirds on either side of the sternum, and separated the heart from the right lung. The tumor was white in color and firm in consistence, although it showed in its interior numerous soft necrotic areas. The pericardial cavity contained about eight ounces of reddish serous fluid and an irregular nodulated mass had grown through the upper part of the sac by direct extension from the parent mediastinal tumor. The auricles also were each invaded through the upper posterior part of the wall by a large polypoidal mass, which, in the case of the right auricle, hung down in the cavity nearly to the orifice of the inferior vena cava. The right lung was also extensively invaded by direct extension from the region of the root, without there being any isolated metastases. Probably, as the result of vascular obstruction, there were numerous infarcts in the right lung. The right bronchial glands, also some of the glands along the right side of the bodies of the upper dorsal vertebræ, and some of the glands in the lower part of the right side of the neck, were considerably enlarged from tumor infiltration. In no part was there any direct connection of the tumor with any bony structure, nor were there any isolated metastases through the rest of the body. The esophagus, trachea, aortic arch, and pulmonary artery were in practically their normal relationships, and although embedded in tumor substance were not obviously invaded in any part. The channels of the larger veins involved in the tumor seemed clear, although the lumen of the right innominate and azygos major veins appeared very compressed.

Microscopically, the growth is a lymphosarcoma of a comparatively active growing type. The component cells are slightly larger than normal lymphocytes, both in their nucleus and cytoplasm. Extension is chiefly along the lines of the lymphatics, and this is associated with a marked surrounding zone of inflammatory reaction. When an air alveolus of the lung has become penetrated by tumor cells, its lining cells generally appear swollen up, and frequently are observed to be desquamated and also to be highly phagocytic to the invading tissue.

As regards the origin of this growth, it would seem to be derived from the lymphatic gland structures of the mediastinum, or possibly from the thymus gland. It has been considered by Kaufmann and others that growths of the lymphatic glands of the mediastinum more usually produce metastases and are more nodular than are growths from the thymus. Virchow also stated that thymus tumors were particularly liable to invade the pericardium. In relation to the possibility of this tumor having its origin in the thymus gland, and considering the known reciprocity in activity between the thymus and thyroid, it is interesting to find that the thyroid in this case was very considerably enlarged, measuring 4.5 cm. vertically in both its lobes. It was quite distinct from the tumor growth and, both grossly and microscopically, presented the proliferative appearances characteristic of the thyroid in exophthalmic goiter.

The specimen illustrating syphilis of the lung was obtained at the autopsy on a woman, forty-four years of age, who had been admitted to the hospital in a very stupid semi-comatose state and with convulsive movements of the hands. Practically no history was obtainable, beyond the facts that she had been troubled with pains in the head and legs for seven years, and that she was a very heavy drinker.

She was a married woman and had had three children, all of whom died in infancy. There had been no miscarriages. As regards the occurrence of syphilis, nothing whatever could be found out. While in the hospital she was noticed to have albuminuria, and a week after admission deep coma developed, and she died in a state of convulsions.

At the autopsy it was noticed that she had very numerous definitely syphilitic scars over the forehead, limbs and trunk. Most of these scars were old, but several over the buttocks were more recent in appearance, and over the outer part of the right buttock there was a large area of ulceration into the subcutaneous tissues.

The kidneys were very small and granular, being in an advanced state of chronic productive nephritis. There was also a

very extreme degree of general arteriosclerosis and the brain was very edematous.

The liver was somewhat smaller than normal, and its surface showed extensive fibrous perihepatitis. Its interior showed a slight degree of early cirrhosis, and microscopically it was evident that the fibrous tissue was of comparatively recent date, and that there were unusually large perivascular lymphocyte collections in this fibrous overgrowth.

The spleen was somewhat atrophic and showed a considerable increase in the thickness of its fibrous stroma.

On opening the pericardial cavity, it was found to contain about six ounces of clear, slightly blood stained fluid, and that the entire serous surface was covered by fibrinous lymph in which organization was just commencing. The tongue presented no smooth atrophy, nor was there any special change in the larger air passages. The bronchial glands were slightly enlarged and pigmented.

Neither pleural cavity contained any fluid, nor was there any evidence of recent pleurisy. Numerous old adhesions, however, united the two surfaces of the pleura, and the lower lobe of the right lung was inseparable from the corresponding vault of the diaphragm. The left lung was, as a whole, very emphysematous; in the upper lobe there was a large patch of gray hepatization pneumonia, and irregularly through the lower lobe there were also some small bronchopneumonic areas, several of which had broken down into small abscesses. The lower lobe presented a very dense reticulum of old fibrous tissue. This fibrous formation was much more condensed at the extreme lower margin of the lung, and in this position quite large areas of the lung appeared to be almost completely fibrous. The upper lobe was practically free of this fibrous overgrowth, save in its lower part, where only a very delicate reticulum was present.

The right lung showed almost similar changes, but the fibrosis in the lower part of the lung was even more dense. An area, about 2 cm. long by 1 cm. broad, at the extreme lower mar-

gin of the lung and attached firmly to the diaphragm, seemed almost uniformly fibrous in composition. An inch and a half above the lower posterior margin of the lung, a long scar extended from the surface deeply into the interior. There were several other scars, not quite so large, which extended in from the surface into the interior of the lung in its lower part, and which evidently were the results of cicatrization of gummata. Throughout this right lung also there were several patches of bronchopneumonia and a few abscess foci also were present.

Microscopically, the pneumonic areas appeared to be ordinary pneumococcic gray hepatization areas, and the breaking down foci contained some staphylococci, as well as pneumococci. There were no tubercle bacilli obtainable in any part of the lung, nor indeed were there any histological appearances of tuberculosis to be observed. The stroma of fibrous tissue, which pervaded the lower lobes of the lung, seemed for the most part to be composed of comparatively dense fibrous tissue, which included occasional distorted acinus-like air alveoli, and also very evident perivascular lymphocyte nodes. In some places obliterative processes in the vessels were also a prominent feature. Besides this old standing fibrous deposit, there were also the connective tissue elements were very young, and the air alveoli in these areas showed a varying degree of distortion, and the lining cells of most of them were markedly swollen and sometimes desquamated, giving an almost adenomatous appearance to the tissue. All gradations between this early connective tissue overgrowth and the dense fibrous bands, which contained only a few distorted remnants of the alveoli, could be observed.

In conclusion, there is no doubt in my mind that, notwithstanding the fact that spirochetes could not be demonstrated, this fibrosis was syphilitic in origin.

This idea is based on several facts, such as the distribution in the lower lobes of both lungs in a patient who was definitely syphilitic. Also on the formation of such extensive scars, and particularly in the case of the right lung, the fibrous mass which involved the diaphragm, and the thick cicatrices just above it

in the lung substance. The fibrosis also appeared older and more irregular in distribution and in histological appearance than what is commonly seen as a result of ordinary productive pneumonia, or from what might be imagined to follow any pleurogenic condition.

Microscopically, there was evidence of some continued process, as there were such great variations in the ages of the reactive inflammatory tissues. The vascular changes also were in favor of a syphilitic lesion.

The fact of this being a primary syphilitic process seems to me more correct than to consider it as a secondary result of a pneumonia which, on account of a syphilitic tendency, has occasioned subsequent fibrosis.

Discussion.

Dr. R. Grace, referring to the case of mediastinal tumor, asked whether the edema of one side of the face and neck was ascribed to organic obstruction, or to some result of the growth, as toxemia, or whether it was to be considered angio-neurotic in origin.

Dr. H. Oertel asked whether any member present had ever seen a similar combination of thyroid tumor and mediastinal growth.

Dr. J. H. Larkin said that three or four years ago Dr. Collins had removed a tumor from the suprasternal notch in a woman who had difficulty in breathing. He had made quite a large incision and taken out a lot of tissue, which on examination proved to be of thyroid origin. The operation was undertaken to relieve dyspnea; the pressure was so great and the position of the tumor such that to remove it was impossible. Three or four months later the woman died with a marked infiltration of the mediastinum. This was apparently a rapidly growing tumor of the mediastinum with marked thyroid characteristics. This was the only time he had ever found thyroid

tissue invading the mediastinum, and it had all the evidences of a malignant growth.

Dr. OERTEL said that one could not recognize the mediastinal growth as being of thyroid derivation in this case.

Dr. LARKIN said that he had simply cited the case as being suggestive—the rapidity of the growth after operation, and subsequent death. There might have been another tumor there at the time, which they had had no means of determining, but the case was very suggestive in view of the beautiful specimen presented.

Dr. F. C. WOOD said that he had seen a large mediastinal growth of the thymus with some hyperplasia of the thyroid, but not to such a degree as this. There was a very large mediastinal growth, but it was from the thymus gland, and was not a lymphosarcoma.

Dr. MILNE said that although there were certain veins in the thorax which were obstructed, yet it was not easy, anatomically, to account for the unilateral edema.

Proceedings

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New York Pathological Society.

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DR. HORST OERTEL, *President.*

REPORT OF TWO CASES OF ADDISON'S DISEASE.

B. C. CROWELL, M.D.

The widespread interest in Addison's disease at the present time perhaps justifies the report of two cases presenting many interesting features.

My first case is that of an Italian married woman, thirty-nine years of age, a shopworker, who was under observation for only forty-eight hours before death. The history was that of good health until three months previous to admission to the hospital. She then had severe pain in the abdomen and back, which for a time became less severe, and was accompanied by sleeplessness and loss of appetite and strength. After two

months her weakness became so severe as to confine her to bed; at this time she had abdominal pain, vomiting, hiccough, insomnia, constipation, and headache, and in the last three months she had lost thirty pounds in weight. Her hands and face grew darker during the last month.

While under observation the essential features which were noted clinically were pigmentation (to be described in the autopsy protocol), marked asthenia, weak pulse (B. P. 84 mm. Hg), and signs of apical tuberculosis. She had an antemortem rise of temperature to 104.2° F., and died with pulmonary edema.

The autopsy was performed thirteen hours post mortem, and was limited to an abdominal incision, through which I was able to remove the thoracic viscera. Externally she was a well nourished woman with brownish pigmentation of the face, back of hands, lips, and gums. She presented the external features indicating status lymphaticus, with the single exception that the hair was more abundant than would be expected in this type in a woman of her age.

The gross anatomical diagnosis was: Chronic fibro-caseous tuberculosis of both adrenals; pigmentation of skin; chronic adhesive pleurisy and pericarditis; healed apical pulmonary tuberculosis; healed tuberculosis of bronchial and retroperitoneal lymph nodes; lymphoid hyperplasia of stomach and intestines; chronic parenchymatous nephritis; chronic salpingitis and ovaritis. No accessory adrenals and no thymus gland were found.

This diagnosis was supplemented microscopically as follows: Tuberculosis of thyroid (weight, 35 grams); tubercles in liver and spleen; hypertrophy of islands of Langerhans (weight of pancreas, 75 grams). The left adrenal was small and very firm, and on section none of the normal markings of the gland could be distinguished, the gland substance being completely replaced by large, white, partly caseous masses. The right adrenal was considerably enlarged, its surface being pale and nodular. On section, there were seen few remains of the markings of the gland, the cortex being represented by faint yellowish

streaks. At the lower pole was a large caseous focus, and surrounding the entire cortex, for a width greater than that of the normal gland, there was pale firm tissue containing a few caseous foci. Microscopically, the adrenals showed complete destruction, being entirely replaced by a central caseous area surrounded by tuberculous granulation tissue, containing some tubercles and areas filled with plasma cells.

The second case was that of a Canadian farmer, thirty-four years of age, who at three years of age had a lesion which was represented by a complete ankylosis of the left hip. He had had bronzing of the skin for eleven years, and had lost twenty-five pounds in weight in the three months previous to entrance to the hospital, where he sought admission on account of weakness, soreness of the muscles, and loss of appetite. Aside from his ankylosed hip, pigmentation (to be described later), asthenia, soreness of the muscles, and low blood pressure (85 mm. Hg), nothing remarkable was noted clinically.

At the autopsy, which was performed two and a half days post mortem, he was found to be still well nourished, with marked bronzing of the skin of the head, face, and dorsum of the hands, and pigmentation of the lips, buccal mucosa, and glans penis. He also presented numerous symmetrically distributed, circular, macular lesions, about 7 mm. in diameter, some with pigmented margins, over the trunk and extremities, in front and behind.

The gross anatomical diagnosis was: Caseous tuberculosis of adrenal glands; chronic coxitis (tuberculous ?); chronic adhesive pleurisy; chronic ossifying myositis of gluteus medius (left); hyperplasia of lymphoid tissue of lingual and pharyngeal tonsils, pharynx, larynx, spleen, and small and large intestines; congestion of lungs; status lymphaticus. No accessory adrenals were found. There was no arterial hypoplasia.

Microscopically, the adrenals showed the same complete fibro-caseous destruction. The semilunar ganglia were large and contained chromaffin: There were some small cervical nodes containing healed tuberculous areas. The pancreas weighed

sixty-five grams, and showed no pathological change; nor did the thyroid, which weighed forty-five grams. The thymus, which weighed twenty-one and a half grams, showed marked hyperplastic changes. One parathyroid, which was sectioned, was found to be the seat of a very extensive fibrosis showing only small remnants of the gland embedded in the fibrous mass. This is a condition which I have not seen described elsewhere.

A third case occurring in our laboratory some time ago, and already described by Dr. Pappenheimer in connection with status lymphaticus, was that of a woman of thirty-two years, who had a typical clinical history of Addison's disease. She presented at autopsy: Diffuse bronzing of the skin; pigmentation of mucous membranes; tuberculosis of both adrenals with complete destruction of the medulla and only microscopic rests of the cortical substance; tuberculous spondylitis; general lymphoid hyperplasia; arterial hypoplasia; a ten gram thymus.

It is interesting to note that these three cases all show signs of a status lymphaticus, in view of Hedinger's published observations of seven out of fifteen cases of Addison's disease associated with status. Hart and Wiesel have also emphasized this coincidence, and Wiesel reports a case of an eighteen-year-old man who died while swimming, and who was found to have a large thymus and an hypoplasia of the chromaffin system. To the latter Wiesel ascribes his sudden death, rather than to his status lymphaticus.

As to the causation of Addison's disease, about the only generally accepted theory is that it is a disturbance in the chromaffin system, of which the adrenal is supposedly the main depot. Addison's original tenet, that tuberculosis of the adrenals covers all, has been found wanting.

Lewin in the study of 370 cases of typical Addison's disease found:

Typical cases of Addison's with sound adrenals........12 per cent.
Typical cases of Addison's with diseased adrenals......88 per cent.
Diseased adrenals without bronzing....................28 per cent.
Diseased adrenals. with bronzing......................72 per cent.

He also mentions forty-four cases of destruction of the adrenals by various diseases in patients dying of intercurrent affections who had had no evidence of Addison's disease during life.

That even tuberculosis of the adrenals does not always cause Addison's disease is shown by numerous cases, as, for example, a case reported by Wiesel of a sixteen-year-old girl who had no symptoms of Addison's in spite of extensive tuberculosis of adrenals, kidney, bladder, and genitalia, and abundant chromaffin cells in the solar, suprarenal, and hypogastric plexuses, and in the ganglia along the vertebral column. Wiesel holds that Addison's disease is a disease of the chromaffin system and not of the adrenals alone; while Karakascheff holds that the disease is due to destruction of the cortex of the adrenal. He reports a case of complete destruction of the medulla by an old hemorrhage without Addison's.

At the present time these seem to be the two main views in reference to Addison's disease. Karakascheff is very strongly of the opinion that the cortex of the adrenals can not be destroyed without producing Addison's, and explains reported cases on the ground of accessory adrenals composed of cortical tissue. He also reports some interesting cases of Addison's disease following destruction of the adrenals sequent to thrombosis of the adrenal veins.

The question, to what extent the extra-adrenal part of the chromaffin system can compensate for entire destruction of the adrenal part, is one difficult to settle, as the bounds of the chromaffin system are being constantly extended by different observers, and some of the parts already described are somewhat inaccessible in the ordinary autopsy dissection. Recently the heart and ovaries have been said to contain chromaffin cells. But it may perhaps be open to question also whether all of our staining reactions are really specific; that is, whether there are not some chemically similar substances which give the same reactions.

There have been several physiological methods devised for determining the presence of adrenalin.

1. The first and best known of these is that of Oliver and Schaeffer, who first described the angiotonic effects of extracts of the gland on intravenous injection.

2. Ehrmann found that the pupil of the excised frog's eye dilates in the presence of adrenalin in dilutions as high as 1 in 10,000,000.

3. Meyer's reaction is dependent upon the contraction of portions of excised vessels when subjected to adrenalin.

4. Lastly, Comessatti has described a colorimetric reaction when adrenalin and mercuric chloride are mixed in certain proportions.

Oliver and Schaeffer found the extracts of the adrenals in two cases of Addison's disease inactive as far as the blood pressure raising reaction was concerned; and in the September number of the *Archives of Internal Medicine*, Wells and Greer have shown the extracts of two hypernephromata to be inactive by the first, second, and fourth tests.

Using the method described by Wells and Greer, I made extracts of the adrenals of my second case, and found that intravenous injections of 2 c. c. produced no rise in blood pressure in the rabbit—this being tried with each adrenal mass independently—while an extract of a healthy adrenal obtained four and one-half days post mortem, and prepared in exactly the same way, produced a distinct sharp rise when 0.5 c. c. was injected.

To show that adrenalin if present in the caseous adrenals could not have been masked in this experiment by a possible depressor action of any of the products of caseation, I injected a rabbit intravenously with a similarly prepared extract of some caseous mesenteric glands obtained from a tuberculous infant and found no change in blood pressure produced.

Similarly, the extract of the caseous adrenals produced no dilatation of the excised frog's eye in several hours, while the healthy adrenal extract produced temporary dilatation as did adrenalin chloride in 1 in 10,000 solution.

W. H. Schultz, of the Hygienic Laboratory of the Public

Health and Marine-Hospital Service, has recently said that naked eye readings of the pupil are of little value, and has devised an elaborate apparatus for observing the pupil and making accurate measurements under constant temperature and light. But I think my observations are not entirely devoid of value, as they were made simultaneously under identical conditions of temperature and light, and the independent readings of four observers coincided.

The solution of the cause of Addison's disease will probably not precede a much more accurate knowledge of the interrelations of the various ductless glands, suggestions of which are coming from the physiologists. Falta conceives of the adrenals as being active in the mobilization of carbohydrates, which are oxidized by the pancreatic secretions, and believes that in many cases of diabetes, besides an insufficiency of the pancreas there exists a primary increase of carbohydrate mobilization by means of a hyperfunction of the chromaffin system. Thus, the adrenals and pancreas are related. The thyroids stimulate the sympathetics, which form a part of the chromaffin system, and the parathyroids depress them. Thyroidectomy in dogs prevents adrenalin glycosuria and diminishes the angiotonic effect of adrenalin, while thyreoparathyroidectomy increases the glycosuria.

The relation between the hypophysis and the genital organs is well recognized, and pancreatic disturbance, manifested by diabetes, is not infrequent in acromegaly, which is probably due to a hyperfunction of the hypophysis.

In my cases there are many factors to consider. In the first, we have found destruction of the adrenals, partial thyroid destruction by tuberculosis, hyperplasia of the thymus, and hypertrophy of the islands of Langerhans. In the second case, aside from the adrenal destruction, we have the thymus and the destroyed parathyroid.

What relations, if any, these bear to one another, and their exact bearing on the clinical course, it is beyond the province of this paper to discuss.

Discussion.

Dr. Charles Norris said that he would like to add a few words upon the intimate connection which evidently exists between status lymphaticus and the diseases of the ductless glands, such as acromegaly, Basedow's disease, and, as had just been shown, Addison's disease. His reason for taking up the subject of status lymphaticus was that in the cases of Addison's disease which he had seen there had been an association with status lymphaticus; but it was a well known fact that the static condition in Addison's was not nearly so marked as it was in the average case of Basedow's, where the condition was usually extremely well marked. He thought that the actual fact was that if the term status were extended to include all cases showing slight or partial lymphoid hyperplasia, it would be found that all Addison's cases had developed in subjects having the lymphatic constitution. He had used the term recessive to designate cases in which the lymphatic hyperplasia was not abundant. In well marked cases of status lymphaticus, the lymphoid hyperplasia was present throughout—in the spleen, the lymph nodes, especially the mesenteric, Peyer's patches, etc. It was his conception of the status lymphaticus that people were born with the static constitution. In this he was borne out by Martels who had dropped the term status lymphaticus and used the term hypoplastic constitution. The recessive theory was beautifully demonstrated in the Peyer's patches, especially in those of adults. In such cases one saw irregular hypoplasia. There were in parts of the patch, tumor-like masses; in other parts, homogeneous scar-like tissue. These areas of scar tissue were found to be made up of hyalin connective tissue. The same thing occurred in the follicles of the spleen, which were transformed into fibrous tissue. As to the external appearance of status cases, Dr. Norris spoke only briefly, but he considered that this lent weight to his theory of a constitutional anomaly. In well marked cases the diagnosis was easy to make. Another thing which confirmed him in his belief that the status was a constitutional anomaly was the association of the status with hypoplasia of the arterial system and of the genital organs.

TERATOMA TESTIS.

JAMES EWING, M.D.

In the text books on surgery and pathology, one finds under the heading of tumors of the testicle a considerable list, including fibroma, myxoma, myoma, chondroma, sarcoma, lymphadenoma, carcinoma, teratoma, and mixed tumors. This classification is based largely on the work of Langhans, who was one of the first to classify testicular tumors according to microscopical structures. He recognized most of these classes as separate, but one of his contributions to the subject was the identification of the so-called alveolar sarcoma of earlier writers with carcinoma.

Wilms, in 1896, took up this subject and concluded that there was a close relationship between several of these tumors. Wilms examined various types of mixed tumors and found that they were all tridermal in structure, and he claimed that all such tumors had an identical pathogenesis. He recognized in many of the teratomata, areas of carcinoma, sarcoma, chondroma, and myoma, and he observed also in some instances that the main bulk of the tumor might be composed of any one of these elements. He even suggested that all tumors of the testicle composed exclusively of one of these elements might be of teratomatous origin; but he declined to assert that such was the case and accepted two definite classes of testicular tumors: one derived from teratoma, and one from the adult elements of the testicle. However, he recognized the indications which the study of teratomata gave as to the possible identity of most of the tumors of the testicle. Since Wilms' time further study of the groups has shown one important principle which Pick has emphasized strongly: that is, the tendency toward the preponderance of one element in teratomata. In the case of the myomata especially, suspicion was early aroused that rhabdomyoma might represent a one-sided development of a teratoma, and Ribbert showed from his study of three cases of rhabdomyoma that they were all portions of teratomata in which the other ele-

ments aside from the muscle had been suppressed. In the same way it has been generally agreed that chondroma of the testis exists only as a one-sided development of a teratoma in which other elements have been suppressed.

So that beginning with this extensive series we may now eliminate as separate tumors, myoma and chondroma.

A few cases of pure fibroma of the testis have been described in the literature, and are possibly genuine. They are so scarce, however, as to have no clinical significance.

As for myxoma, no genuine cases of pure myxoma of the testis have been described in the literature.

Lipoma is sometimes mentioned. There is no case of pure lipoma of the testicle on record, although this tumor is rather common in the spermatic cord, where, however, it is often associated with teratomatous elements.

While many of the adenocarcinomata are supposed to be derived from the seminiferous tubules, genuine pure adenoma of the testicle is almost never seen. Adenoma is practically limited to portions of the mixed tumors, and a pure simple adenoma of the testicle I have not been able to find, with one exception. Pick and Chevassu report cases of multiple adenomata in undescended testes. Three or four small nodules in the body of the testicle were found, looking like solid, well circumscribed, fatty areas. The tissue was made up of neoplastic seminiferous tubules; and it was believed to be the only true adenoma of the testicle. The conclusion, therefore, is that true adenoma of the testis arising in the seminiferous tubules exists, but is very rare and of no clinical importance.

In sarcoma one has to deal with a more complex group. Alveolar sarcoma figured largely in the diagnoses of the older surgeons, but Langhans showed that this tumor belongs with the common carcinomata. A famous group of sarcoma has been described, by French observers especially, under the term "sarcome angeioplastique." In recent years it has been shown that this tumor is identical with the growth aping the chorionic structures, and may properly be called a chorioma of the testicle.

There are a number of side lines of evidence which led to the recognition of these tumors as identical with chorioma. It has been shown that these choriomata are portions of teratomata and that they are often composed of all three germinal layers, so that chorioma as a simple tumor may also be thrown out.

Lymphadenoma has a lengthy history, especially in French literature. It is usually described as round celled sarcoma, often as a small round celled sarcoma. It was pointed out by Malassez as a highly malignant growth composed of small round cells, and called a specific type of sarcoma. The latest German writers also refer to this growth and they are somewhat undecided as to its exact significance. The most competent discussion of lymphadenoma is that by Chevassu (Thèse de Paris, 1908). He points out that in the reports of lymphadenoma of the testicle the size and shape of the cells vary, that the stroma is not always present, and that the clinical history does not always show differences from that of carcinoma of the testicle. He has himself examined several cases now standing in French literature as lymphadenoma and he has concluded that they are a form of carcinoma, and he states that the pathologists who made some of these diagnoses have stated to him that they have changed their opinions. He concludes that lymphadenoma as a primary tumor of the testicle does not exist. So that in the opinion of the most competent French observer this type of tumor is now eliminated from the group of primary neoplasms of the testicle. I have felt that many of the cases in the French literature were not genuine cases of lymphadenoma, and I was partly prepared to accept Chevassu's conclusions. Therefore, under the heading of sarcoma a third group may be struck out.

We now come to a little more difficult field, that is, the spindle celled sarcomata. There are about six or seven cases in the literature which one can not eliminate; some of them are old, some recent. The most satisfactory case is the one reported by Chevassu in 1907, which was of large bulk, and was composed chiefly of spindle cells with mucoid stroma and many giant cells. He studied all portions of the tumor, but failed to find

any other element. He would not state positively, however, that this was a pure spindle and giant celled sarcoma of the testicle, but said that it might perhaps be a mixed tumor. The later literature contains a number of cases of spindle celled sarcoma, but the descriptions do not read in a straightforward manner. There are a number of features about the descriptions which make me think that it would be wise to defer judgment as to the occurrence of this tumor in the testicle in pure form.

Hansemann described a tumor which he derived from the large interstitial cells of the testicle. His article was brief and the descriptions were incomplete, and it would seem that he intended more to suggest the possibility of the existence of such a tumor, rather than to make a positive claim. Not much attention has been paid to the interstitial cell tumors of Hansemann, but they have been classed among the sarcomata. The existence of such a tumor has not been demonstrated at the present time. The most recent contributions show that at times the interstitial cells multiply to such an extent as to produce a tumor-like process, but never reach the grade of a genuine neoplasm. Chevassu and others have discussed the part played by interstitial cells in sarcoma of the testicle and their conclusion is that there are no malignant tumors of this origin, that the forms of hyperplasia observed are more or less functional.

There remains then simply the old round celled sarcoma of the testicle, large or small, alveolar or diffuse. This is the commonest diagnosis made to-day on tumors of the testicle. There are different views in regard to the nature and origin of this tumor. Probably most writers at present believe that the round celled sarcoma is a carcinoma of the embryonal type derived from the cells of the seminiferous tubules. Chevassu thinks that he can demonstrate the origin from cells lining the seminiferous tubules. He admits that he could not trace the tumor directly to the lining cells of the tubules, but on general grounds he concludes that they are derivatives of these cells. He finds that the tumor cells exactly resemble certain cells of the tubular lining, but he lays stress upon the fact that this tumor develops within

the testis, supplants testicular tissue, and remains inclosed in the tunica albuginea for a long while. It would seem that Chevassu and others are assuming too much. The morphology of the cells of this tumor is not sufficient proof that they have developed from the lining cells. Moreover, one must remember Ribbert's opinion, that one can not tell from the examination of advanced tumors what relation the cells of origin bore to the surrounding tissues.

From the study of a series of cases I have reached the conclusion that all the common carcinomas and large round celled tumors of the testicle, including the "seminome" of Chevassu, are one-sided developments of teratomata. My opinion is based chiefly upon specimens of two cases which I have to show. One of these is a tumor of the testicle, which was received with the diagnosis of gumma, but which proved to be an interesting teratoma. This tumor consisted of two main portions: one a solid fibrous part, the other a soft medullary carcinomatous part. Several cross sections of a fibromuscular and glandular organ were found in the hard part. There were three lobules of tissue identical with normal adult human thyroid. I am aware that Aschoff has warned against fantastical interpretations of such findings, but I am confident that the fibromuscular organ in this teratoma was either a deformed uterus or possibly a stomach. I am, however, much inclined to consider it a uterus. Such an organ has not been previously observed in these tumors, nor has the presence of thyroid tissue been previously described. Here there are two adult organs, one possibly a uterus, the other certainly thyroid tissue, while the entire mass was surrounded by a diffuse carcinoma of a very characteristic type commonly seen in teratoma of the testicle. This carcinoma is characterized by the presence of large polyhedral cells supported by a stroma richly infiltrated by lymphocytes, the stroma appearing to be an integral part of the tumor. As to the explanation; one possibility is that we are dealing with two tumors, one giving rise to thyroid and uterus, and the other to the carcinoma or the seminome of Chevassu. The other possibility is that the tumor is a

teratoma of which the different elements have given rise to both
portions of the tumor. The latter explanation seems to me to
be preferable. In order to assume that the carcinoma was de-
veloped from the seminiferous tubule cells, one must suppose
that he is dealing here with two distinct tumors.

The second original case on which I base my conclusions
is a very early tumor of the testis in a physician, thirty-seven
years of age. This tumor was about 1 x 2 cm. in size, and was
composed of two portions separated by a mass of fibrous tissue.
Portion 1 is typical chorioma. Portion 2 is typical large celled
carcinoma, and in the center there is a small area of fibro-carti-
lage with a few canals lined by high cuboidal epithelial cells.
There is no question that this is a tumor of Wilms' type, since
it contains derivatives of all three germinal layers. The reason
why cases showing this type of carcinoma have been separated
from teratoma is that in them nothing but carcinoma has been
found. Here is a very early case of carcinoma in which a small
island of cartilage was found together with chorioma. It seems
quite probable that if either one of these epithelial elements had
been allowed to grow it would have suppressed the mesodermal
structure, and would have been the only apparent element in the
tumor. Fortunately this case was obtained very early, and thus
its teratomatous nature was recognizable. I can not, therefore,
accept Chevassu's conclusion that his carcinoma was derived
from the seminiferous tubules, since I have found in one such
case an island of cartilage indicating a teratomatous origin. This
conclusion is offered as an hypothesis which can be worked
upon, and I am gathering more material for study in this direc-
tion.

If this very complex group of tumors of the testicle can
be simplified in this way, the question arises whether similar
principles do not apply in other regions, and this possibility
seems to lend increased importance to the study of testicular
tumors.

The conclusions reached are briefly as follows:

The tumors occurring in the testicle are: fibroma, spindle

celled sarcoma, multiple adenoma, and teratoma with its derivatives.

Pure fibroma, spindle celled sarcoma, and adenoma are very rare; teratoma is common.

Myxoma, myoma, chondroma, carcinoma, and large round celled sarcoma or carcinoma occur in the testicle only as onesided developments of teratomata.

Discussion.

DR. W. G. MACCALLUM said that although he had been attacked by everyone who had written on testicular tumors since the publication of his own case, he had not taken further occasion to refer to it. Dr. Ewing had gone through the whole list of tumors of the testicle, and had ruled out one tumor after another as being after all of teratomatous nature. It seemed that a line of division might be drawn between teratomatous tumors as such and those in which one element of the teratoma, instead of remaining merely distorted tissue, had taken on the peculiar characters which are distinctive of invasive malignant tumor growths. In this sense it was very difficult to say that any malignant tumor was not primarily of teratomatous origin. In the case to which he had referred, the tumor consisted apparently of one type of tissue in addition to the loose myxomatous stroma. It was typically a malignant tumor growing with extreme rapidity into the veins and extending widely throughout a great part of the venous circulation, even filling up the jugular veins and some of the cranial sinuses. Although it was perfectly possible, and perhaps probable, that this tumor arose primarily from misplaced embryonic structures in the testicle, there was nevertheless the typical alteration in these tissues which gave it its malignant character. In view of this fact, it seemed hardly more necessary to speak of this tumor as a teratoma than to apply the term to most other malignant growths. The conditions would have been very different had other types of tissue been found in the primary growth. Dr. MacCallum thought that the group of

tumors mentioned by Hansemann offered a field of especial in-
terest in the determination of their origin, for it would be neces-
sary, since they seemed allied to the interstitial cells, to deter-
mine whether or not they were mere hyperplasias of these cells
before classing them with sarcomata or other tumor subdivi-
sions.

REGENERATION OF LIVER TISSUE.

LINDSAY S. MILNE, M.D.

This subject, which has undergone such varied and exten-
sive discussion, may frequently be well illustrated in many dis-
eases of the liver. One of the best examples of the phenomena
of compensatory reformation of liver tissue occurs in the dis-
ease known as acute liver atrophy, and is especially evident in
its more subacute types.

Cases of acute liver atrophy vary greatly in their clinical
histories and also, in more or less corresponding degree, in their
pathological appearances. In the cases in which the patient suc-
cumbs early in the disease, the essential histological feature is a
widespread necrosis of liver tissue. In slightly more protracted
types, the destroyed liver cells begin to disintegrate and disap-
pear, and the capillaries between which they lay become in cor-
responding degree dilated. The skeleton of the lobule, in con-
sequence of this liver cell destruction, tends, to some extent, to
collapse and, in accordance with the duration of the disease, a
new formation of connective tissue spreads into the destroyed
lobule from the region of the portal spaces. As the duration of
the illness increases, owing possibly to a better resistance of the
patient or to a less virulent type of the disease with less exten-
sive liver destruction, the necrotic tissue becomes more com-
pletely replaced by fibrous tissue, until eventually, in the late
types, only islets of liver cells are included among extensive
areas of fibrous tissue.

In the subacute stages of the disease, the remaining unde-
stroyed liver cells can be observed to have assumed a very active
hyperplasia. To illustrate some of the different stages and ap-
pearances of this subacute type of liver atrophy, I may, in brief,
present three cases which occurred in children. At this time of
life the subacute variety seems to be relatively the prevalent type
of the disease.

Case 1.—Occurred in a well nourished boy, six years old,
who had died after an attack of gradually deepening jaundice
of eight weeks' duration, with no other particular symptoms
having been observed, save those of apparent heart failure to-
ward the end. Even at the time of death the jaundice had not
assumed any very marked degree. At the autopsy, the liver was
slightly reduced in size. As a whole, it was dark red in color,
but on its surface were several large, irregular, slightly elevated,
bright yellow patches. On section of the organ, these yellow
areas were rather ill-defined and were irregularly arranged
among a red, firm tissue. The bile passages showed no particu-
lar abnormality.

Microscopically, the yellow areas proved to be liver cells
which had apparently escaped destruction, and although some
were somewhat degenerated, they were for the most part in an ac-
tively hyperplastic state. The lobules were larger than normal
and more irregular in outline, while the individual liver cells
forming the trabeculæ had apparently also become very irregu-
lar in size and shape, some being large and pale from hyper-
trophy, others small, darkly staining both in cytoplasm and nu-
cleus and arranged in clumps.

There were also numerous giant cells, each containing sev-
eral nuclei. Occasionally karyokinetic figures were seen in the
liver cells, but evidences of amitotic cell division were much
more common. Apparently every stage of this latter process
could be observed, independent of any phase of karyokinesis.
This process consisted apparently of a swelling of the nucleus
and cytoplasm followed by a condensation of the chromatin, fis-
sion of the nucleus and a subsequent cleavage of the cytoplasm.

In this process of rapid amitotic liver cell division multinucleated giant cells appeared to have been formed frequently, and there were some evidences that they also sometimes seemed to have split into clumps of small, darkly staining liver cells.

The intervening red substance between the yellow areas was composed of skeleton lobules made up of distended capillaries from which the liver cells had been completely removed. The lobules were somewhat collapsed, and a new growth of young, cellular fibrous tissue from the portal spaces had replaced about half or more of the outer part.

Case 2.—Occurred in a very well nourished girl, four years old, who had succumbed after a forty-day history of progressive jaundice with practically no other special coexisting symptoms. Twenty months previously she had suffered from a somewhat mild attack of jaundice of two months' duration. She died of gradual heart failure and without any supervening cerebral symptoms. The autopsy revealed a liver somewhat less in size than normal, extremely firm, and of a dark red color. Projecting on the surface, particularly near the portal fissure, were a considerable number of large, rounded, bright green colored, tumor-like masses of varying size up to that of a walnut. In the interior of the liver also there were numerous large, well defined, green areas.

Microscopically, the green nodules were found to be composed of liver cells, extremely irregularly arranged, partly degenerated, but showing numerous signs of recent and also of old hyperplasia. Many of the liver cells were large, irregular and evidently hypertrophic, and large numbers had assumed the appearances of giant cells; as many as thirty nuclei being present in some of them. Nuclear division by amitosis and also rather frequent karyokinetic figures could be observed. The intervening fibrous tissue was rather dense and had completely obliterated all lobular structures. Possibly in this case the initial destruction had taken place two years previously, coincident with the first attack of jaundice. Some more recent toxic change had destroyed the balance of liver tissue and so led up

to the terminal issue, and had also been responsible for the evident recent signs of degeneration and of recent liver cell hyperplasia.

A common type is also illustrated in a well developed girl six years and eleven months old, who presented a history of an attack of jaundice a year previously, since when she had occasionally complained of diffuse pains over the epigastrium. For the last seven weeks she had been looking sick and the development of ascites had been noticed. During the last five days of life she had been slightly jaundiced and she had been getting increasingly torpid. She died after having been comatose for a day, during which time she had also frequent convulsive movements of the face and extremities. At the autopsy a large amount of ascitic fluid was found in the abdominal cavity. The liver was extremely small, being of a pinkish-gray color, and from its surface there projected numerous, irregular, fairly large, well defined yellow nodules. These nodules were composed of masses of closely packed liver cells having no trabecular arrangement and individually being very irregular in size and shape. The intervening tracts of fibrous tissue were very dense and contained only a few rather attenuated "ducts." Both macroscopically and histologically the appearances in this case were too uniform to simulate an ordinary coarse cirrhosis, which naturally is very irregular, owing to its being due to a long continued, frequently repeated damage to small areas of liver tissue and not to a widespread, rapidly accomplished destruction as in acute and subacute liver atrophy.

In ordinary atrophic cirrhosis of the liver, the extremely complicated picture which is seen of collections of irregularly arranged and variously shaped liver cells included in tracts of fibrous tissue is not altogether due to a simple replacement of areas of necrotic liver substance by fibrous tissue, but compensatory liver cell hyperplasia is also to a large extent accountable.

Besides the rapidly accomplished destruction of liver tissue which occurs in acute liver atrophy, and that which occurs more slowly giving rise to common cirrhosis, all other extensive dam-

ages to the liver are apt to be associated with evidences of liver cell hyperplasia, being especially marked when the volume of the liver is seriously reduced somewhat rapidly. In a case of leukemia, I have seen large numbers of liver cells in karyokinetic division as well as very frequent evidences of ordinary amitosis. Around lymphadenoma nodules in the liver in one case there were enormous numbers of liver cells in all phases of mitosis. The liver cells, in this case, around the nodules were in an extremely active state of hyperplasia. Almost similar appearances may often be seen around multiple malignant tumors in the liver. In such conditions as chronic venous congestion, where a great deal of liver tissue has become lost by atrophy, there are commonly apt to occur extensive signs of liver cell multiplication and particularly hypertrophy. In conditions, then, demanding compensatory increase in function of the liver cells, there is apt to be both a hypertrophy, and also a multiplication of liver cells directly and with no transition in type through "bile ducts" or other means. The main method of cell division is by amitosis, although mitosis in the early generations of liver cell new formation can fairly commonly be observed.

Experimentally, compensatory liver cell regeneration can also easily be demonstrated. This regeneration depends largely for rapidity and for extent of development on the amount of liver tissue removed. Thus in the rabbit, three weeks after removal of half the liver, the remaining half, throughout, shows very marked evidences of regeneration. The lobules are very much larger than normal, some of the individual liver cells, particularly those towards the periphery of the lobules, being very hypertrophic, while others, mostly near the intermediate zone, seem to have split into a large number of small, darkly staining cells. Mitosis in this new development, again, is only rather rarely seen, and, I think, occurs to a marked extent only in the early stages. Amitosis, as also apparently in human conditions, seems to be the method by which the main part of the new liver cell multiplication is accomplished. In twenty-four to forty-eight hours after removal of half the liver in rats and rabbits,

the liver cells at the periphery of the lobules are evidently enlarged, pale and hypertrophic. From the fourth to the eighth day evidences of new formation of liver cells can generally be distinguished, and during this period karyomitotic figures may fairly frequently be observed. In two to four weeks the multiplication of new liver cells is at its maximum.

Another method of liver cell regeneration is commonly accredited to the small, "bile-duct structures" which are frequently noticed ramifying amongst the fibrous tissue in numerous pathological conditions of the liver. These have very commonly been considered as at least an attempt at new formation of liver cells. These "ducts" are seen well in all recent developments of fibrous tissue, as in subacute liver atrophy and in certain of the more acute types of cirrhosis, while in chronic dense fibrous formations they are either very fine or cannot be observed at all. In the well-defined strands of fibrous tissue in old quiescent atrophic cirrhosis, for example, there are often none of these "ducts" to be observed. In acute liver atrophy, and also in all kinds of recent inflammatory change in the liver, they can often be seen in direct communication with old interlobular bile ducts. Their lining epithelium is generally very regular in type, but sometimes shows catarrhal changes and may form small, club shaped masses of cells. The neck where the new structure joins the interlobular bile duct is usually rather fine, or lined by a very regular type of epithelium, and I have never seen any definite evidence that these ducts are derived by a proliferation or sprouting from an interlobular bile duct: Undoubtedly, catarrhal proliferative changes do often occur in these interlobular bile ducts, as one would expect from the action of the irritants, necessarily associated with most pathological conditions of the liver, being eliminated down them. Artificially also catarrhal changes may be produced with marked multiplication of the lining cells by the injection of pancreatin, etc., into the bile ducts, or as the result of general toxic administrations. In these proliferative states, no signs of sprouting out of duct-like structures can be observed. Serafini has also shown the remarkable rapidity and

completeness of regeneration of the epithelium of the bile passages. As a result of his experiments, it appears that in eight days after the lining membrane of the gall bladder has been scraped off, a new epithelium had completely reformed.

These "ducts" have also been considered to be derived from atrophied liver cells, but in conditions of atrophy from chronic venous congestion, in waxy disease, in congenital syphilis, etc., the atrophying liver cells do not really closely resemble the fresh-looking, regularly lined "ducts" familiarly seen in fibrous tissue developments in the liver. Experimentally, also, transplanted pieces of liver of the same animal do not show in their regressive changes any condition resembling the "ducts." Out of a series, in only two rats did the implanted liver cells persist for any considerable time. In these the liver cells could still be recognized after three months. They had not proliferated at all and were very considerably split up by inflammatory cells.

In certain cases of liver cirrhosis these apparently new "ducts" are found in great numbers, and by serial sections they can frequently be traced into interlobular bile ducts and also directly to trabeculæ of liver cells, and they generally join either of these structures more or less abruptly, with no transition in type of lining cell. A good case illustrating these connections was observed in the liver of a child four months old, who had died after an attack of jaundice which had lasted since the day after birth, and was due to a congenital obliteration of the bile ducts. In this case the liver was greatly enlarged and intensely bile stained. The peripheral part of each lobule was occupied by a zone of young fibrous tissue, in which ramified enormous numbers of bile-duct structures. These "ducts" with great frequency communicated with the interlobular bile ducts, easily distinguishable from them, however, as they were lined by a somewhat different type of epithelium, and as the latter frequently possessed a very delicate elastic lamina. They also, with even greater frequency, communicated with liver-cell trabeculæ having a lumen perfectly continuous with the intratrabecular bile collecting canaliculus. Even in one high-power field of the mi-

croscope, these "ducts" could sometimes be seen joined to both an interlobular bile duct and to a trabecula of liver cells, there therefore being a complete excretory channel from the liver cells. Their epithelium was very regular in type, except sometimes just at the communication with liver cells or bile ducts, at which places it occasionally tended to appear fine, rather like a capillary. The extremely tortuous and ramifying character of the "ducts" in this case, as also in other pathological conditions of the liver of children, may to a large extent be explained by the well-known irregular and branching course of the connecting bile canaliculi in the small livers of early childhood as compared with the more direct character prevailing in the fully developed adult liver.

It might seem then as if these "ducts" were simply the becoming more evident of normal bile canaliculi, isolated from their normal envelopment of liver cells, and in their new environment having assumed this larger type of lining epithelium. Similar processes to this can also be seen in the flattened lining cells of the air alveoli of the lung in conditions of interstitial pneumonia, in Bowman's capsule of the glomeruli in various kidney diseases, etc.

I might also briefly mention another case of subacute, or what might be called chronic, liver atrophy which appeared to be somewhat illustrative of these processes. It occurred in a fairly well-nourished man, aged forty-one years, who had died after an eight-months' history of mild jaundice, which had, however, begun rather acutely. He had no particular gastrointestinal symptoms, with the exception of hematemesis, during the last week of life. There was, however, a history of nephritis and cardiac failure for fifteen months, and for the last five months there had been a gradually increasing ascites. He died of purulent peritonitis. The liver, at the autopsy, was found to be enormously reduced in size, weighing only 700 grams and measuring only 6 cm. in thickness in its central part. Its surface was smooth, as a whole, but especially on the upper part of the right lobe and near the hilum numerous brownish-green no-

dules of varying size projected. The interior of the liver was mainly made up of pink-colored, firm fibrous-like tissue and embedded in this were scattered, irregular, brownish-green masses. Microscopically, these latter areas were composed of closely packed hyperplastic liver cells. The intervening fibrous tissue was dense and contained relatively few "bile ducts." In some few parts, however, there were considerable numbers of rather attenuated "ducts." Here some recent toxic process seemed to have destroyed the liver cells which previously occupied this area. The trabecular structure and approximately normal capillary arrangement could still be made out and the intratrabecular bile canaliculi which had in large part escaped this destruction appeared in some places as fine, undifferentiated tubes, sometimes being slightly dilated; in other places they had a lining of very flattened endothelial-like cells, and in still other places the epithelium had assumed a cubical definitely "duct" appearance. There were then in these areas apparently all stages in development of definitely cubical lined "ducts."

In cirrhosis of the liver the apparently new "ducts" are commonly seen either to end in a clump of definite liver cells, or else to have fully formed liver cells included in some part of their course. At first sight it would seem as if the "ducts" were forming the liver cells, or possibly that the liver cells were originating the "ducts," or even that the "ducts" might have some purposive quality of growth attempting to connect liver cells with interlobular bile ducts. It seems easier, however, to understand, in the absence of proliferative evidences, that the liver cells thus included in, or in relation to the end of, the "duct" are merely the old pre-existing liver cells and that the "duct" has become more evident simply as a result of a change in type of the epithelium lining the collecting canaliculus, which has resisted the destruction responsible for the removal of its enveloping liver cells.

Experimentally, also, the function and fate of these "ducts" may be studied, in wounds made in the liver. Their appearance does not seem to be dependent on the amount of damage done

to the liver, as is seen to be the case in liver cell multiplication.
They may be seen frequently at the edge of the wound in four
or five days, often in connection with exposed ends of liver cell
trabeculæ which do not seem to show any definite evidences of
proliferating them.   They may also be seen in the neighborhood
of portal spaces, involved in the edge of the necrosis and to be
carried irregularly outward from these positions by the develop-
ment of new inflammatory tissue.   At first they are always fine
and somewhat like a capillary, but soon their epithelial lining
cells swell up and the familiar "duct" is to be seen.   In three
or four weeks these "ducts" are usually most definite.   They get
progressively more distorted from their normal positions by the
development of inflammatory tissue, but after six weeks they
begin to show signs of atrophy.   In two or three months they
are usually very atrophic-looking, and often no more can be seen
than in the fibrous tissue strands of a quiescent type of cirrhosis.
They seem then to be derived from a swelling up of the lining
epithelium of the normal canaliculi leading from the liver cells
to the interlobular bile ducts.   These structures are naturally
more resistant to destructive influences than are the liver cells
and, persisting in their new inflammatory environment, assume
the well-known regular "duct" type.   Their lining epithelial cells
may occasionally show proliferative changes, but these are due
to catarrhal changes induced by irritants in process of elimina-
tion inside the "duct," or to the proliferative changes which
might be expected in this epithelium disturbed in its normal
function and involved in a new environment.

Regeneration of liver cells takes place very freely, follow-
ing any rapid extensive reduction of liver tissue and is accom-
plished by a multiplication of pre-existing liver cells, chiefly by
amitotic division, the early phases apparently also being initiated
by the karyokinetic method.

Discussion.

DR. RICHARD M. PEARCE said that he had been particularly impressed with the great resemblance between this lesion and that which he had described some time ago in the dog, caused by the use of hemagglutinative sera. In the first place, the acute lesion produced experimentally was microscopically very much of this type. There, also, large areas of liver were destroyed. In the second place, the mitosis of liver cells took place at about the same distance from the necrosis; that is, in about the third or fourth row of cells from the area of destruction. The giant cell formation occurred to a wonderful extent in these animals, and could be explained only by an atypical type of proliferation of liver cell nuclei about necrotic cell fragments. What their fate was he did not know. He gathered from what Dr. Milne had said, that in this human lesion the cells split up into smaller cells, and he would be very glad if Dr. Milne could say something more about the fate of these cells: whether there was a further cell division or not into fairly typical liver cells. In regard to the bile-duct question, Dr. Pearce said that although he considered the formation of liver cells from the newly formed bile ducts to be the more common condition, in some of his lesions he had felt that there could be traced a transformation from true liver cells into these so-called false ducts. In the experimental lesion a very large portion of these newly formed ducts were essentially solid cell processes, and as such he did not see how they could be interpreted as the remains of pre-existing ducts; they must be considered as the result of proliferation of pre-existing ducts and analogous to the angioblasts of granulation tissue.

DR. W. G. MACCALLUM thought that studies of such cases as were referred to by Dr. Milne showed pretty clearly two methods of regeneration of liver tissue: one in which the remaining liver cells gave rise by mitosis to new liver cells; and the other a less perfect method and one usually cut short by the death of the patient, a new formation of liver cells by the

sprouting of the bile ducts. The mitotic division of the liver cells appeared almost simultaneously very soon after the primary injury, while the proliferation of the bile ducts seemed to go on much more slowly. The structures commonly spoken of as newly formed bile ducts in cases of regeneration after acute yellow atrophy and in cases of cirrhosis of the liver seemed to him to be really newly formed bile ducts, at least in part; while in part they were the remains of the more resistant original ducts. In their growth they might fulfil two ends, either to reestablish connection with the newly formed liver cells, or to form at their budding ends new liver cells. In one or two cases of very advanced cirrhosis of the liver it had been possible to demonstrate this to his satisfaction, inasmuch as the cells of the liver tissue in general were deeply pigmented while the bulbous masses of new liver cells on the ends of the sprouting bile ducts were evidently fresh and stained pink without any pigmentation. In some cases mitotic figures could be observed in these bulbous ends. This was particularly evident in one case in which after extensive destruction of the liver cells the skeletons of the lobules remained intact, and into the site of the old liver cells such bile ducts could be seen sprouting radially from all sides of the lobule.

DR. PEARCE said that he did not wish to be understood as stating that the formation of bile ducts from liver cells was a common process; on the contrary, he considered it a most unusual process.

DR. HARLOW BROOKS said that he had been extremely interested in this presentation, but he had disagreed with some of the conclusions. Dr. Milne had stated that the clinical picture of these cases was identical with cirrhosis. Dr. Brooks' experience had been confined to three cases, only one of which had come to autopsy. This was absolutely not the same condition. He believed that in the next few years, after more careful study, it would be possible to make a sharp differentiation, on the one hand from acute atrophy of the liver, and on the other from cirrhotic conditions. In the first place, in cirrhosis the vascular

changes and symptoms are pronounced. In these cases, so far as he had seen, the vascular symptoms do not occur. On the other hand, they were sharply differentiated in the lack of toxic conditions so manifest in cases of acute atrophy and infective icterus. These cases were strikingly free from symptoms of poisoning which one associates with practically all acute degenerative processes in the liver. There was also an absence of fever and an absence of the urinary findings which one gets in acute atrophic conditions. He thought that this was a distinct disease which could be recognized by its clinical symptoms.

DR. JAMES EWING said that he was much interested in the clinical aspect of these cases. He had always felt that the scope of the term acute yellow atrophy of the liver was very much wider than the textbooks indicated. There were a large number of cases occurring in subjects who recover, and he thought that it would be a distinct advance when the particular clinical conditions which lead to acute yellow atrophy of the liver followed by recovery were recognized by the clinicians. Dr. Ewing had seen conditions clinically in which he felt that a very considerable destruction of liver had occurred, and yet the patient recovered. It seemed to him that the clinical side of this study was quite as important as the study of the minute anatomical changes.

DR. BROOKS said that the histories of these cases had been studied very carefully. The patient referred to was an intelligent man who was in the wards for four months, and who absolutely denied any such acute attack, as it was thought he must have had. On the other hand, he never showed any signs of getting well; he grew steadily worse.

DR. HORST OERTEL said with regard to the relationship of bile ducts to liver cells, that, while his study of the experimental lesions was limited, in a considerable study of human lesions he had never seen any pictures which indicated to him a transformation of bile ducts into liver-cells. He had at times seen specimens which might impress one as a transformation of liver cells into bile duct epithelium; but of late he had become doubtful

about that transformation.   He had formerly been accustomed
to speak very liberally of bile duct proliferation; but he had
been much impressed with Dr. Milne's study and it appealed to
him particularly because it had considerable analogy to paren-
chymatous changes in other productive inflammations.   In the
productive and tuberculous inflammations of the lungs, for in-
stance, no one would think that the transformation of alveoli
into glandular loops represented newly formed structures, but
old alveolar epithelium, which under changed environment had
changed its form.   Similarly in the productive nephritis, we re-
gard the new adenomatous loops, so frequently found, not as
new productions, but old tubules and cells which, under changed
surroundings, have changed their type.   One hesitates to accept,
still, the old idea of so-called excessive bile duct proliferation in
productive hepatitis and the transformation of liver cells into
bile ducts.   Without absolutely denying the latter, Dr. Oertel felt
quite strongly that this was not a general process.

Dr. Milne said that the early cases which he had described
showed nothing more in the clinical histories than a gradual de-
velopment of jaundice.   The child whose illness had lasted six
weeks felt perfectly well up to within a few days before death.
There was no other condition than jaundice; no pain or other
symptoms.   In regard to the giant cells, Dr. Milne said that
there were some evidences that they split into a number of small
cells.

A PRACTICAL IMPROVEMENT IN THE PREPARA-
TION OF ANILIN-GENTIAN-VIOLET STAIN.*

BY JULIUS SHARNOSKY.

(Laboratory Helper, Bellevue Hospital.)

Paltauf's modification of the anilin-gentian-violet solution
was called to my attention by Prof. William Elser.   I have been
unable to find any reference to a published description of the

*Read in abstract by Dr. Charles Norris.

method, but learn that it has been in use for many years in Vienna.

The advantages of this staining fluid consist in the uniformity of its preparation, its permanence, and the absence of precipitate upon the slide. The formula for its preparation, and the time limits for the staining with this solution and with Gram's iodine solution and absolute alcohol (for all of which I am indebted to Dr. Elser) are as follows:

> 3-5 cc. Anilin, Merck's.
> 90 cc. Distilled water.
> 7 cc. Absolute alcohol.

Shake thoroughly; filter through moistened filter paper, and make sure that solution is clear. Then add

> 2 g. Gruebler's powdered Gentian Violet.

Allow fluid to stand for twenty-four hours, on account of precipitation which takes place. Filter before using.

The solution is good only when a metallic lustre develops on the surface of the fluid. This solution is said to keep from four to six weeks in a stoppered bottle which has been thoroughly cleaned.

Application:

Anilin-water gentian violet. . . . . 3 minutes.
Gram's iodine sol. 2 minutes.
Absolute alcohol, with stirring. . . . . 30 seconds.
Weak carbol-fuchsin, or aqueous fuchsin. . 30 seconds.

The times stated above should be strictly adhered to, and the preparation should not be washed in water until the counter staining is finished.

The great importance of the anilin-gentian-violet stains in routine bacteriological work has led to a series of experiments with a view to improving them, especially with regard to permanency. The difficulty in preparing Gram's stain is well known. The disadvantage consists in not always obtaining a clear solution of anilin oil in water, the stain, when finally pre-

pared, keeping at most two weeks, at the end of which period it begins to lake, complete deterioration taking place. In large laboratories the annoyance of continually having to prepare fresh stains, and the frequent necessity of waiting till a fresh product can be prepared, made the desirability of conducting experiments with the first stated view in mind most keenly felt.

As a result, a stain has been produced embodying both stability and ease in preparation. This was accomplished through the use of a salt of anilin, instead of the base. This salt is a white crystalline body, much more soluble in water and in alcohol, yielding a clear solution, and possessing, at the same time, a higher grade of stability. The formula, as finally developed, is given below, together with a comparative table of the different anilin-gentian-violet stains in use.

Formula:—Dissolve 3.5 g. of anilin hydrochloride (Kahlbaum's) in 90 cc. of water; add 10 cc. of absolute alcohol; warm to about 60° C. and add 1 g. gentian violet slowly, with constant stirring; digest over a small flame for about 10 minutes and filter.

It will be seen that the characteristic metallic luster develops at once, thus doing away with the necessity of waiting twenty-four hours before the stain is ready for use. The product prepared as above has kept ten months to date, without the slightest signs of deterioration.

Perhaps it would be advisable to say a word regarding the addition of 10 cc. of alcohol. In the old formulas, alcohol, of course, serves to facilitate the solution of anilin. But one may very properly question the necessity of using alcohol in our formula, in view of the solubility of the anilin salt in water.

If we start out with the premise that the anilin hydrochloride, when purchased, is absolutely neutral, there is no reason for the addition of alcohol. However, the commercial salt invariably has an acid reaction due to hydrolysis, rendering the addition of a few drops of anilin necessary to effect a neutral

reaction,[1] and it is thus apparent that the use of alcohol is desirable.

	Anilin.	Alcohol.	Stain.
Ehrlich's Anilin Gentian Violet[2]..........2.5%-3%		15%	0.5%-1%
Ehrlich's Anilin Methyl Violet[2]..........2.7%		8%	1%
Stirling's Anilin Gentian Violet[3]..........2.3%		10%	1%
Paltauf's Anilin Gentian Violet[4].......... 3%-5%		7%	1%
Bellevue Pathological Laboratory:			

Anilin Hydrochloride.

{Anilin Gentian Violet or
   Anilin Methyl Violet)...............3.5%   10%   1%

(Equivalent to 2.5% Anilin.)

STRIATED CELLS IN THE FETAL THYMUS.

A. M. PAPPENHEIMER, M.D.

Dr. A. M. Pappenheimer demonstrated to the Society a microscopic section of the thymus of a five and one-half months human fetus, showing curious striated cells. So far as he knew, similar cells had never been described in the human thymus. They had the appearance of atypical striated muscle cells, such as are found in the teratomata and congenital rhabdomyomata of the heart. They were spindle shaped structures, most of them long, varying in thickness. The nuclei were oval, large, and situated on the surface. They all showed perfectly distinct cross and longitudinal striations. They were scattered through the lobules, usually occurring in groups, and showing a tendency to lie at the periphery. Such cells were first described by Mayer in 1888, and since then had been found in the thymus of various fishes, amphibians, reptiles, and birds. It had been spe-

[1] The term "neutral reaction" in this case is used from the standpoint of congo-red and fuchsin, and not as regards litmus or methyl orange.

[2] Either gentian violet or methyl violet may be used in either of these formulas, although methyl violet, on account of its greater purity, is to be preferred.

[3] Formula calls for 5g., but 1% (1g.) actually dissolves.

[4] Formula calls for 2g., but 1% (1g.) actually dissolves.

cifically denied that they ever occurred in the mammalian thymus. Their significance has been a matter of dispute. The majority of authors explain them as fetal inclusions. Other writers have considered them peculiarly specialized cells derived from the reticular epithelium of the thymus. These cells, according to Hammar, show a pretty definite fibrillar connection with reticular cells. Dr. Pappenheimer was inclined to agree with Hammar's view. One reason was that in this same thymus he had found rudimentary Hassall's bodies which consisted of two or three cells, some of the individual fibrillæ showing distinct cross striations. In other places, there was a connection between these fibrillæ and the reticular cells. The term "myoid cells" had been suggested for these structures.

A detailed description of these cells, with literature, will appear in the *Journal of Medical Research*.

DOUBLE HYPERNEPHROMA.

B. C. CROWELL, M.D.

Dr. B. C. Crowell showed a large tumor which had been removed at autopsy from a patient at Bellevue Hospital. The patient was a young girl, eighteen years of age, who had been admitted to the hospital in a practically moribund condition, so that but little history could be obtained. She said, however, that she had never been strong, though she had had no illness except typhoid fever. She had always been small. On admission she was found to be very much emaciated, the loss of weight having taken place within the last four months. During that time she had noticed an enlargement of the abdomen. She thought that at times her urine had been cloudy and bloody, and she had had some pain on urination.

At autopsy she was found to be much emaciated, with this very palpable tumor which lay on the left side practically dis-

placing everything, the kidney being pushed downward. The growth did not originate in the kidney itself, which was apparently intact except for slight metastases in the lower pole. The tumor had undergone extensive necrosis, and aside from the general appearance there was a considerable amount of fluid which looked very purulent, as though infection had taken place. Section of the anterior part showed a tumor juice exuding from it on pressure. A similar smaller tumor occupied the site of the right adrenal, displacing the kidney tissue downward. The ureters and bladder were perfectly free; there was no ascending infection. The kidneys showed minute abscesses, and abscesses were also found in the intestine and spleen. Metastases were present in the kidneys, in the retroperitoneal lymph nodes, and in the pleural viscera up to 3 cm. in diameter. Some very small nodules were found in the substance of the left lung. Section of the vessels was very unsatisfactory on account of the size of the tumor, so that whether or not there was tumor tissue in the renal veins or vena cava could not be determined.

The tumor was presented as a hypernephroma which was interesting on account of its large size, the two masses together with the kidneys weighing thirteen pounds.

A CASE OF PRIMARY TUMOR OF THE VELUM WITH MARKED COMPRESSION OF THE FOURTH VENTRICLE.

HARLOW BROOKS, M.D.

The patient was a girl aged eleven years. She first came under observation of Dr. J. Constantine MacGuire, to whom I am indebted for the history and most of the clinical notes of the case. The child was born of nervous and excitable parents and from early life had been the witness of constant domestic disturbances, so that the nervous condition that she presented had

been looked upon as fully accounted for. She had suffered from various diseases of infancy, and had always been considered frail, although of about normal size and development for her age. Previous to coming under the care of Dr. MacGuire, she had been ill for two weeks, suffering from a condition diagnosed as "brain fever."

On examination she showed general muscular rigidity of a spasmodic character with slight opisthotonos. She rolled and tossed about the bed, was illogical, and had at times to be restrained. Occasionally she screamed and cried hysterically. She complained rather persistently of pains in the head. The knee jerks were accentuated; there were no ocular disturbances manifest; and examination of the eye grounds was said to be negative. There was no Babinski reflex; and no elevation of the temperature; and the pulse varied from rapid to slow. At this time a diagnosis of probable meningitis was made.

The child was removed from the surroundings which were manifestly bad for her condition and was placed under observation in a hospital. Here she was actively purged and put upon vigorous doses of the bromides. Under this treatment the symptoms apparently entirely cleared up, the muscular rigidity passed away and the child was soon able to sit up and to walk about the ward. Mentally the condition became apparently normal, cerebration and speech were quick and apparently natural in every way and the patient was cheerful and uncomplaining. Medicinal treatment was then entirely suspended, but the child remained under observation. With this startling result following treatment naturally a diagnosis of hysteria was made.

Some days after apparent recovery, a parent of the child was permitted to see her and, unknown to the attending physician, brought a detective who sharply questioned the child as to alleged misdoings on the part of the other parent. The girl became very much distressed and excited, and shortly after this ordeal developed convulsive attacks of the same nature as those previously present, during which she soon died.

Post-mortem examination shortly after death showed a

practically normal condition throughout the entire body except for the following lesions in the brain which are quoted verbatim from the protocol.

The skull, scalp, and dura mater are entirely normal, but the blood vessels of the pia arachnoid are moderately injected. The markings of the brain are regular, symmetrical and typical. The convolutions are, however, remarkably flattened, and palpation of the hemispheres shows fluctuation. On removal of the brain from the skull the infundibulum was found to be greatly distended and on its rupture about 500 cc. of clear cerebrospinal fluid escaped. The sella turcica is somewhat excavated as a result of the infundibular distention, but the pituitary body is apparently normal. The optic chiasm is compressed by the bulging infundibulum, and its bands are thinned and slightly atrophied.

The foramen of Munro is greatly dilated, and on opening the lateral ventricles they are found to be enormously distended with cerebrospinal fluid. The choroid plexuses are anemic, but otherwise apparently normal.

Section through the cortical tissue of the cerebrum shows marked anemia but otherwise, aside from compression, it is apparently normal. The cortical gray matter is normally thick and regular.

Section of the pons, medulla, and cerebellum shows a large tumor mass apparently originating from the velum which covers in the floor of the fourth ventricle. As a result the floor of the ventricle and superjacent substance of the cerebellum are greatly compressed, but neither tissue appears to be integrally invaded.

On careful dissection the tumor can be readily separated from the cerebellum, but not from the floor of the fourth ventricle where it is firmly attached by a more or less clearly defined adhesive pedicle which covers in almost the entire ventricular area. The tumor is flattened oval in form; it measures six cm. in diameter, and three cm. from above downward. It is light

pink in color, very soft, and almost pultaceous in consistence; but it shows no areas of gross necrosis.

The superjacent cerebullum is very much compressed, but no areas of invasion or of degeneration can be made out in it. No strands of degeneration are grossly demonstrable in the tracts of the lower medulla or in the cervical cord, although the ventricle of this portion of the cord is somewhat dilated. The tumor has completely obliterated by compression, the iter and the passage below connecting the medullary ventricle with that of the cord; this is doubtless the explanation of the condition of hydrocephalus.

Microscopic examination of the tumor shows it to be composed of a diffuse mass of embryonic connective tissue cells which are for the greater part of the small round cell type. The stroma is very scanty and is largely composed of spindle-shaped cells which are evidently closely related to those which make up the chief mass of the tumor. Blood vessels are infrequent, but the tumor is rich in what are apparently lymph passages. The smaller channels are composed of irregularly arranged tumor cells, and only the larger vessels show a definite structure into which adult connective tissue and endothelium enter.

Portions of the velum are still intact in the growth, though the neoplasm has evidently sprung from the connective tissues of this structure. No direct evidence of invasion of the tissue of the cerebellum or medulla can be made out.

Histologically, I am inclined to class this tumor as a sarcoma of the small round cell variety, but in some respects it resembles a glioma. Taking into consideration, however, its evident point of origin, I believe that I am fully justified in the assumption that the growth is a sarcoma. From a clinical standpoint the case is chiefly interesting and remarkable in that with so marked a growth complete relief of symptoms took place from time to time. It is, of course, absurd to assume that the bromide had directly to do with this amelioration, but I am rather inclined to the idea that the catharsis with the mental quiet and rest which the child enjoyed after removal from her home

were partly responsible for the cessation of symptoms. It is, however, possible that the inhibiting action of the bromide on the activity of the ganglion cells really may have had a share in causing this improvement.

Manifestly, the convulsive and irritative symptoms manifested by the patient when she was first seen were due to the acute hydrocephalus. It is probable that with the rest in bed and quiet of the hospital a certain amount of absorption of this fluid with relief of the cortical pressure took place, as a result of which the temporary improvement noted occurred. It also seems probable that the excitement induced by the painful questioning of the sensitive child caused a cerebral hyperemia, with perhaps increased secretion of the cerebrospinal fluid, increased cortical tension and resulting convulsions and death.

It is extremely difficult to understand why choked disk, Babinski reflex, and other evidences of cerebral compression were absent in this case. The absence of disturbances of equilibrium with such marked cerebellar compression is truly remarkable, but no more so than the absence of respiratory and cardiac disturbances when the floor of the fourth ventricle was so universally and remarkably compressed.

In so far as I have been able to determine. the case is unique, not only in symptomatology, but also in the location and character of the tumor. As a whole, it only verifies the quaint statement said to have been made by Charcot: "There is no lesion of the central nervous system which may not exist at times without symptoms and there are no symptoms which may not appear without lesion."

Discussion.

Dr. F. C. Wood spoke of an autopsy which he had seen at St. Luke's Hospital, during which a brain tumor was found which had given few symptoms. The case was that of a woman, apparently perfectly healthy, who had been in the hospital for about a week, and had been given large doses of acetanilid and sulphonal. She died very suddenly, it was supposed from the effect of the drug. She had been very nervous and had complained of headache; nothing else had been noted. At autopsy the tumor, a large glioma, was found in the left parietal region.

THE DIFFERENCES NOTED BETWEEN HUMAN AND BOVINE TYPES OF TUBERCLE BACILLI: SUGGESTIONS FOR THE SIMPLEST METHODS OF DIFFERENTIATION.

CHARLES KRUMWIEDE, JR.

(From the Research Laboratory, Department of Health, New York City.)

The following work was undertaken to determine the type of bacillus in different forms of tuberculosis. It has been done under Dr. Park's direction with the aid of several other workers to carry out the technical part of the investigation. A full report of the details of the work and those concerned in it will be published later. About six hundred cultures have been studied. These were from four hundred and twenty-eight cases of tuberculosis in man, and thirty-one specimens of bovine origin.

Methods of Isolation:—No direct cultures were attempted. All material was injected into guinea-pigs which were allowed to live from three to five weeks. At the end of this period the tuberculous organs were removed and thoroughly minced with knife and forceps. This minced tissue was then smeared over the surface of the culture tube. This mincing and rubbing of the material over the culture media we have found preferable to simply cutting the tissue, laying it on the surface of the media and subsequently moving to spread the growth as advised by Theobald Smith. The second opening of the tube, a fruitful source of contamination with moulds, is avoided, and the final growth is equal or greater in amount.

Methods of Cultivation:—Egg media of two types have been used for isolation and further cultivation. The ease and simplicity of preparation and the uniformity of the final product make other media for isolation unnecessary.

The egg media were made as follows: Plain egg (Dorset): the whole egg was mixed with 10 per cent. by weight of water and inspissated at 70 C. for two hours in a closed moist chamber. A few drops of sterile water were finally added to each

tube to provide the necessary moisture.   Glycerin egg (Lube-
nau) consisted of ten eggs mixed with 200 c. c. of 5 per cent.
glycerin bouillon, 1.5 per cent. acid to phenolphthalein and coagu-
lated as above.   Eggs were secured which were quite fresh.

Other media, as glycerin agar, glycerin bouillon and gly-
cerin potato were also used to determine the cultural character-
istics and for further cultivation.   The glycerin potato has been
the most uniformly successful as a stock medium for further
cultivation.   The cotton stoppers in each case with or without
dipping in paraffin were pushed down the tube, which was then
closed with a tight-fitting charred cork and incubated in the in-
clined position.

Nearly all the cultures so far isolated have fallen into two
distinct groups, eugonic (luxuriant) and dysgonic (sparse).
This difference is noticed on plain egg, but to a less marked de-
gree than on glycerin egg.   Here the influence of glycerin on
the growth of the two types, as noticed by several investigators
and carefully elaborated by Cobbett, causes a wide gap in the
amount and rapidity of growth of the two types.   The dysgonic
type commonly fails to grow in glycerin egg from animal tis-
sue and if transplanted from plain egg after the first or second
generation grows but sparsely.   The growth consists of thin,
flat spreading colonies 1 to 2 mm. in diameter, or of a confluent
thin, flat, slightly granular, non-pigmented layer, which is usu-
ally moist.   The eugonic type, on the other hand, grows luxuri-
antly in most instances on glycerin egg, directly from the ani-
mal tissue and in every case in the second and third generation.
The growth is confluent, raised, and crumpled, or coarsely ver-
rucose and dry, and, in practically every case, shows a pink pig-
mentation in early generations.   The pink color depends on cer-
tain unknown differences in the different batches of media.

The other media used, as glycerin agar, potato, and bouil-
lon, we have found mainly of value as corroboration of the
above differences for the following reason : The eugonic strains
grow luxuriantly upon these media usually in the second genera-
tion and with few exceptions in the third and fourth.   The dys-

gonic strains, on the other hand, usually fail to grow in the early generations, or if they do the growth is very slight.

The differences in the growth of the two types as given apply only to the first few generations and to cultures which are three weeks old, the rapidity of growth as well as the amount being an important factor. In later generations and with longer periods of incubation the differences are not so extreme, and in a few cultures the gap is closing.

The above description and division into distinct and widely separated types of growth is true of the majority of cultures. There are, however, as would be expected in such closely related varieties of the same species of organism, a smaller number of cultures which tend to bridge the gap between these diverging cultural types. At the present time the following classification seems warranted, though further study may make some changes necessary.

Human Type: Group 1.—Glycerin egg: Grade 7 to 8 in the first three generations and pigment on glycerin egg mixtures in the early generations. Glycerin potato: Grade 6 to 8 in the first four generations.

Group 2.—Glycerin egg: Same as Group 1. Glycerin potato: (a) Less than Grade 6, or (b) negative or slight, in first four generations.

Group 3.—Glycerin egg: Grade 4 to 6 with pigment slight or absent in first three generations. Glycerin potato: Grade 3 to 5 in first four generations.

Group 4.—Glycerin egg: As in Group 3. Glycerin potato: Negative or practically so in first four generations.

Group 3 and 4 show no marked increase in amount of growth in the first ten generations.

Bovine Type:—Group 1.—Glycerin egg: Grade 0 to 3 for first three generations; negative or slight, directly from the animal tissue and growth remaining sparse for at least ten generations. Glycerin potato: Slight or negative in the first four generations.

Group 2.—Glycerin egg: Grade 2 to 4 for first three gen-

erations. That is, the growth is better than Group 1, and is usually positive directly from the animal tissue, but not increasing very much in amount in the first ten generations. Glycerin potato: Slight or very moderate growth in the first four generations.

Group 3.—At first as in Groups 1 and 2 on both glycerin egg and potato, but rapidly increasing in amount of growth in the first ten generations reaching Grade 6 or even higher, and showing some pigmentation on reaching the higher grades.

In explanation of the above grouping, the grades of growth refer to the total amount as judged by inspection of the cultures. In each case the best growing tube of any set was considered the typical one. Nine grades were arbitrarily selected; thus: Grades 1 to 3, sparse; Grades 4 to 6, moderate; and Grades 7 to 9, vigorous. The reason for the selection of glycerin egg has already been spoken of. Besides albuminous media of this type we wished also to select some media which would contain no coagulable albumins to serve as a more rigorous index of the saprophytism of the two types. After numerous trials, potato was found to be the most uniform in its results. In some of the earlier cultures before this routine was established other media as glycerin agar and bouillon were used in the early generations, and in these few instances we shall consider them as falling into one of the groups as though potato had been used, as they seem to be absolutely typical in other respects.

When one studies this grouping of the two types there is apparent a gradual graduation from one type to the other. Of the human types no one could mistake Groups 1 and 2 for bovine cultures, nor could they mistake Groups 1 and 2 of the bovine type for human cultures, if they had handled even a few cultures on these media. As to Group 3 of the human type, the difference is still sufficiently marked to make a statement as to type on inspection of the tubes of the first few generations. When Group 4 is reached differentiation is very difficult on these two media, though the fact that the growth reaches its upper limit at the very start points strongly to the human type. Other

media may add some information in these cases, as for instance the ability to grow from glycerin egg on to glycerin bouillon which has been added to the tube, a phenomenon we have not seen in any early bovine culture. Group 3 of the bovine type has been differentiated without exception by the characteristics of the early generations, though one must admit that when the first culture of this type was encountered we considered the possibility of error, but further observation has shown that the early generations, as we thought, are the diagnostic ones. After a few more generations the distinctions in human Groups 3 and 4 and bovine Group 3 are lost and the last tends to outstrip the other two in vigor of growth. These three groups then tend to bridge the gap and form a complete series of types.

This division into two types according to the cultural characteristics has been uniform with the results of animal inoculations, and in practically every case the rabbit virulence has been correctly predicted from the cultural characteristics.

The following is the method we have used in testing the virulence on rabbits: The bacilli are removed from the surface of a subculture which is less than one month old and the excess of moisture is removed by gentle pressure between sterile filter paper before the mass is weighed. The culture medium used for these subcultures, with a few exceptions, has been glycerin egg, and there have been added to the tubes, after coagulation of the medium, a few drops of glycerin bouillon. The growth immediately above the fluid can be readily and perfectly emulsified. After weighing, the bacterial mass is emulsified in physiological salt solution, which is added in such amount that 1 c. c. of emulsion represents 1 mg. of organisms. The dysgonic viruses in many instances afforded too little growth for weighing. An emulsion was, therefore, made and compared with a known emulsion from a eugonic virus, the comparison consisting in the equal ease with which print could be read through each emulsion. A slight amount of saline solution was then added, in order that the error, if any, might fall upon the small side. The amount of fluid inoculated was always 1 c. c. The intravenous

route was decided upon as the most suitable for our purpose, and it has been adhered to throughout the experiment. The dose used has been 1 mg. or 0.01 mg.

It soon became evident that we had to deal with two varieties of organisms, one of which far exceeds its fellow in virulence. An animal inoculated intravenously with 1 mg. or with 0.01 mg. of bacilli of the bovine type soon becomes emaciated, the fur loses its lustre, respiration becomes labored, and death occurs with the larger dose in from seventeen to thirty-eight days with an average period of twenty-one days, and with the smaller dose in from twenty-five to seventy-eight days, with an average of forty-four and six-tenth days. Autopsy reveals extreme emaciation and, except in rare instances,* a generalized tuberculosis involving almost every structure in the body. The lesions in the lymph nodes, and of these particularly the inguinal and the axillary, are almost pathognomonic. The nodes are enlarged, congested and studded with minute caseous areas. The spleen is three or four times its normal size and riddled with tubercles, and the kidneys show on their surfaces an average of from six to ten tubercles each. The liver very commonly contains macroscopic tubercles. The lymph nodes of the abdomen are usually enlarged, as are those of the thorax, and commonly show small tubercles which may be caseous. The lungs are always largely consolidated, and are literally a mass of tubercles. Tubercles on the heart muscles are not infrequent. The duration of the illness is shortened by increase of the dose, but is also influenced by the individual resistance of the animals, nor does it seem that old rabbits are much more resistant than young ones.

Separated from such viruses by a wide interval of virulence are the eugonic viruses. Those never cause generalized progressive lesions in doses of 0.01 mg. or even 1 mg., and a rabbit so inoculated will usually live until carried off by an in-

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*There were four of these rabbits in which the lesions were localized chiefly in the lungs. The same cultures used in the smaller dose produced generalized tuberculosis.

tercurrent malady. The appearance at autopsy is in striking contrast to the findings described in the preceding paragraph. The animal will be found well provided with subcutaneous and abdominal fat, and the lymph nodes, with few exceptions, are normal in size and appearance. The appearance of the lungs varies with the length of time that has elapsed since inoculation. About six weeks after injection they are pretty extensively involved, for at this point, of course, many of the inoculated organisms are arrested. But that the lesions under discussion are regressive is shown by the fact that many animals have gained weight, as well as by our observation that in rabbits autopsied after an interval of three or four months, the lungs are pink, well collapsed, and with tubercles only sparingly distributed throughout them. Almost always there are a few tubercles in the kidneys. The spleen is of normal size, and it is very rare that a tubercle may be found on its surface. Tubercles in the heart muscle are quite uniformly absent. Occasionally after a long interval, there occurs a chronic caseating tuberculous lesion such as orchitis, osteomyelitis, adenitis, mastitis, or large cold abscess.

As in the cultural characteristics of the two types so in the widely divergent types of virulence for rabbits, as described, are included the great majority of cultures. Here also, there are some intermediate grades of virulence apparent. The viruses which show this variation in virulence have not been sufficiently studied as yet to warrant any subdivision of groups as in the cultural characteristics. At the present time, it is impossible to say how far there will be a tendency to fill the gap between the two extremes of virulence. We can say, however, that these variations have not given us any reason to doubt the reliability of the virulence test in rabbits as a means of differentiation when the test is properly controlled by repetition where any variation occurs in one or more rabbits of a series.

Wherever any intermediate characteristics of cultures or rabbit virulence have occurred, the combined evidence of both has left no doubt as to the type of organism.

In a series of selected cultures we have tested the virulence
on young calves. Fifty milligrams of culture emsulsified in 5 c.c
of normal saline was injected subcutaneously in the neck. Here
again the cultures have fallen into two distinct groups. The
human type caused only a local lesion or at most an extension
into the neighboring lymph nodes and had no effect on the
health of the calf. The bovine type on the other hand produced
an acutely fatal generalized tuberculosis. Varying from these
two extremes was the result in one calf receiving a bovine virus,
where a chronic and apparently regressive generalized tubercu-
losis was caused.

The above description has rather accentuated the variations
from the widely separated characteristics of the two types. We
have done this to show plainly the fallacy of working with a few
cultures and then questioning the existence of two distinct types
of tubercle bacilli. This would probably be the result if an in-
vestigator should happen upon several variants in a small series
of cultures. On the other hand if all cultures were absolutely
typical of the two extremes his conclusions would be diametric-
ally opposite. In neither case would his results be true. Our
own conclusions have been modified from time to time, the
earlier work pointing to wide divergence only, the latter work
showing variations from these results. This is really what one
would expect from analogy with other bacteria, viz., that in two
closely related types of organism there is not a wide gap, but
rather two norms around which the two types vary, these
variants in no way causing any doubt as to the existence of the
two types.

From the foregoing descriptions it is evident that the simple
observation of the amount of growth forms a reliable index
of the type in the great majority of cultures. We would suggest
the following simple routine for differentiation using the media
given. First, isolation using egg and glycerin egg, then trans-
planting for three generations at three week intervals on these
media plus glycerin potato, the egg being used because growth
may fail on the other media. All vigorously growing cultures

would immediately class themselves as human, all feebly grow-
ing cultures as bovines. This would dispose of nearly all cul-
tures. The remaining cultures, if any, showing variations from
these extreme types should then be tested in rabbits giving an
intravenous dose of 0.01 mg. If the rabbit survives, kill after
a period of fifty or sixty days, and the generalization or non-
generalization will settle the question of type. As far as the
time limit is concerned we are still experimenting. A safe rule,
however, would be to insist that rabbits survive fifty days and
then show no generalization before the culture be considered
of the human type. Early generations should be used for in-
oculations. It is necessary to say that the utmost care be taken
that the cultures be pure both by microscopic examination and
transplants on ordinary media. A contamination that escapes
one may cause a human strain to simulate the bovine type of
growth.

The above routine if carefully followed gives all that is
apparently necessary to separate the types, although it gives a
limited amount of information as to the characteristics of a cul-
ture. There is always the possibility of a strain giving atypical
results in both culture and rabbits. These cases are in the great
minority and will be noted if above steps are carried out, and
further observations can then be made. Another possible factor
is avian tuberculosis. There does not seem to be any reason for
considering this in view of the evidence that has been advanced.

Discussion.

DR. ALFRED F. HESS agreed that tubercle bacilli could well
be divided into two types and that differentiation between
the human and the bovine bacilli was possible by the first cul-
tures. It very rarely happened that a mistake was made. In
cases where a misjudgment might be made, as where the bovine
type grew particularly well, or the human cultures particularly
poorly, a rabbit inoculation would be sure to show whether the
culture were bovine or human. A great many observers did not

accept this sharp differentiation into human and bovine type; certainly there were some human types which resembled the bovine, and some bovine which resembled the human; but by taking cognizance of the cultural types and virulence, there were no cultures which could not be placed in one group or the other. It was possible that tubercle bacilli could be altered somewhat in their cultural characteristics and virulence in the human body; that a bovine bacillus in the human body for a number of years might grow more luxuriantly and lose some of its virulence. This had never been proved, though it seemed to be the only way to account for some bovine strains which resemble human strains. Dr. Krumwiede had a case where the human and the bovine type were found in one individual. This finding was difficult to explain, as, for example, where the human type appeared in the spleen, and the bovine type in the mesenteric glands, or vice versa. That had given occasion to some for saying that one type might change into another, and was certainly difficult to understand. Dr. Hess spoke of two important facts in the differentiation of the bacilli: First, no case had as yet been reported in which bovine tubercle bacilli were isolated from the lungs; all cases of pulmonary tuberculosis had been of the human type. Second, all cases of bone and joint tuberculosis, with one exception, had been of the human type. So that if one got a primary pulmonary tuberculosis he was pretty safe in saying that the bacillus was of the human type. Yet many believed that bone and joint tuberculosis were of bovine origin. All other tuberculoses had been found to be either human or bovine and could not be charged to one group.

Dr. Krumwiede said that in one case the bovine bacilli had been isolated from the cerebrospinal fluid, and the human bacilli from the mesenteric glands.

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DR. HORST OERTEL, *President.*

A TUMOR OF THE SUBMAXILLARY REGION: A TUMOR OF THE OVARY*

H. S. MARTLAND, M.D.

Dr. H. S. Martland showed a specimen removed at autopsy from a man, thirty-seven years of age, who had died from pulmonary tuberculosis. The specimen included the tongue, larynx, and trachea. At the right of the median line there was an oval, more or less nodular, firm tumor, which was well encapsulated and on gross section had a spongy appearance. The tumor was not vascular, and was light gray in color

*Presented at the meeting of November 10, 1909.

throughout. It lay in the anterior triangle of the neck, and its lower border came just below the bifurcation of the carotids, though it did not straddle the carotid notch nor encircle the arteries. From its microscopical appearance the most probable diagnosis seemed to be perithelioma of the carotid.

In reviewing the literature of carotid gland tumors, an excellent résumé by Keen and Funke was found. Several arguments might be brought forward against the theory that this tumor was one of the carotid gland. It lay anterior and slightly external to the carotid, on the level of the carotid notch. Most of such tumors are described as lying between the external and internal carotids, and often encircling or straddling the notch. It should be remembered, however, that if the growth were glandular it might push upward as it grew and finally lie upon these structures. The tumor was very firm in consistency, and in this particular also differed from most of the carotid tumors, which have been described as of medium firmness. Of course, this would depend largely upon the amount of fibrous tissue and the dilatation of the vessels. The tumor was a light gray throughout, whereas most of the carotid tumors are described as brownish gray to red in color. The tumor was globular in shape, and not lobulated, as are most of the carotid tumors, and no grooves made by the vessels could be found. The microscopical picture, on the other hand, and the presence of red cells among the tumor elements, point to a possible perithelioma of the carotid gland.

The salient points in the clinical history were as follows: The patient first noticed a small lump in the neck when he was twenty-two years of age; for the next two years this grew rapidly, and then for thirteen years remained quiescent; that is, up to the time of his death. The tumor had never caused any pain or discomfort. Before his death the diagnosis of calcified tuberculous glands was made, the mass being a little too high to be considered a cystic or calcified lobe of the thyroid.

Marchand, in 1891, first recognized this tumor; since then

twenty-nine cases were reported up to the year 1906, two of them at autopsy. The increase in the reports of such tumors since 1906, shows that they are less rare than was supposed.

About a year ago, Dr. Martland had had sent to him a tumor which was removed at operation and which proved to be an undoubted perithelioma of the carotid. The patient did well for a time, but died three or four months later from a recurrence at the base of the brain, probably from rests not removed.

The second specimen was a solid ovarian tumor which was removed at operation from a child twelve years of age. The history was as follows: Two weeks previous to admission to the hospital the patient had sharp stabbing pains in the abdomen. Four days before admission the pains had become constant and localized on the right side, and were accompanied by nausea and vomiting. The bowels were very constipated. On palpating the abdomen a large oval mass was felt lying in the median line. This mass was slightly more prominent on the right side than on the left. The blood count showed 20,000 white cells, polymorphonuclears, 86 per cent. A diagnosis of possible appendical abcesses was made, and the appendix was opened. This large mass was found, but the tumor was not removed on account of the extreme weakness of the patient. The acute symptoms were probably due to torsion on the broad ligament. One week later the growth was removed. Adhesions to the great omentum and abdominal wall caused troublesome bleeding, and the patient went into surgical shock. Her condition did not warrant further interference, and a complete operation was postponed for three weeks. At the second operation the left ovary showed no signs of involvment, but three weeks later, when the third operation was performed, the left ovary showed a mass the size of an orange, and there was also extensive involvement of the broad ligament and retroperitoneal glands. The child lived for several weeks after the third operation and died with numerous nodular masses in the abdomen and a pronounced bronchopneumonia.

On gross section the tumor was quite edematous. A large part of the tumor looked like myxomatous tissue, but stained rather deeply and was thought to be edematous connective tissue stroma. There were also large areas in the tumor which resembled hemangio-endothelioma. Whether the blood had ruptured into the spaces or not was not determined. There were besides considerable areas representing smooth muscle; no striated muscle was found. In certain parts there were a great many cysts averaging from 2 to 15 mm. in diameter. These cysts were lined with cuboidal shaped and low cylindrical cells; some contained blood, some nothing but serum. A great part of the tumor, which was grayish or yellowish gray in the gross, microscopically simulated a lymphangio-endothelioma. In some parts typical glandular structures appeared, formed of a single layer of cylindrical cells, the cells being devoid of cilia. The following tissues were not found: cartilage, nervous tissue, fat, striated muscle, and bone.

Discussion:

Dr. F. C. Wood said that although it was difficult to judge of the first case presented by Dr. Martland, without further study, he thought that before making a diagnosis of carotid growth the possibility that this was an ordinary complex tumor of the submaxillary gland should be carefully considered. He thought the presence of cartilage and myxomatous tissue pointed to this diagnosis. The photographs appeared to show ordinary alveoli filled with coagulated matter which stained red with eosin. The carotid tumors which he had seen had been of an entirely different type, showing nothing like this particular specimen.

Dr. Leo Buerger said that he was inclined to agree with Dr. Wood in classing this particular tumor with the mixed cell variety of endothelioma usually found in parotid and submaxillary glands. There seemed to be no question as to the presence of the typical myxomatous and cartilaginous tissue characteristic of these growths. As regards true tumors of the carotid body, he had seen one case. It occurred in a middle aged woman who

was operated upon by Dr. Lilienthal at the Mt. Sinai Hospital in May, 1909. The tumor was about the size of an orange, and was situated at the bifurcation of the carotid artery, being intimately connected with the external and internal carotids and extending upward for a considerable distance towards the base of the skull. The operation was difficult and resection of the common carotid and its two branches had to be done. Microscopically the tumor was a firm fibrous one composed of two main lobules inseparable from the large vessels which were embedded in it. Histologically it was an endothelioma. Although most of the tumors of the carotid body have been reported as being peritheliomas, the fact that chromaffinic cells have been found in them of late seems to throw some doubt upon the previous assumption that the growths are angioblastic. Further study should be directed towards determining whether they do not belong to the neoplasms of the sympathetic system. Dr. Buerger, therefore, wished to ask Dr. Martland whether the reaction for chromaffin cells had been made in his tumor.

DR. MARTLAND said that the cells of the tumor had failed to give reaction for chromaffin.

THE PRESIDENT said that while both of these cases were very interesting and important, it seemed to him, since there was some disagreement as to the diagnosis, that they should be referred to the Committee on Microscopy for further study before the reports were admitted to the records of the Society. He, therefore, requested that Dr. Martland confer with the Committee on Microscopy, and that the committee report at the next meeting.

* * * * *

At the meeting of the Society held on December 8, 1909, Dr. Martland said that after consultation with the Committee on Microscopy he would like to change his diagnosis on the first case which he had presented at the November meeting, and call this an ordinary mixed tumor of the submaxillary gland, probably arising from misplaced submaxillary tissue. The anatomical

position of the tumor was rather low, and this had deceived him as to its nature.

As regarded the second case, a large solid malignant tumor of the ovary in a child of twelve years, which was presented for diagnosis, for the reason that although he had thought it to be teratomatous he wished to know whether it might not possibly be a one or two layer embryoma, Dr. Martland said that the committee had decided that it was probably a three layer embryoma or teratoma.

Dr. F. C. Wood said that from the three sections of the second case which he had seen, while it seemed to him that the epithelial growth did imitate some of the teratomatous tumors, especially those of the testicle, yet he could see only new growth of epithelium. He had found no cartilaginous or other structures which would warrant the diagnosis of teratoma.

Dr. James Ewing said, in regard to this ovarian tumor, that in his judgment it followed the rules laid down for teratoma of the testis and was probably teratomatous. It contained very curious epithelial structures, in some cases approaching the appearance of chorioma, in other places growing diffusely, and in still other places mingling with the stroma, so that in parts it was difficult to determine the line of demarcation between epithelial cells and stroma cells. It contained also cysts lined with high cuboidal cells. The stroma itself was distinctly embryonal. It was formed of mucoid connective tissue with a great abundance of fibroblasts, sometimes so numerous as to approach the standard of sarcoma. It seemed to him that from the general history of ovarian teratomata and the fixed law of predominance of one element in teratomata, the chances were strongly in favor of this tumor being a teratoma.

In regard to the first case, Dr. Ewing thought that one or two points should be emphasized. The first was the long history of the case without operation, the patient dying finally of tuberculosis. Compared with the average course of a parotid gland case, this was rather remarkable. In his laboratory he had notes on the sixth operation on a somewhat similar case extending over

some years. The tendency of these tumors to recur was notorious. Another point was the unusual position of the tumor, which was situated below the inferior maxilla and was closely adherent to one of the carotid arteries, which was unusual for a tumor of the submaxillary gland.

DR. WOOD thought that the recurrence of these parotid tumors was very largely due to the inability of the surgeons to remove the growth completely. If the tumor were free and could be completely extirpated, the result was almost uniformly no recurrence. But most of the tumors were closely entangled with the finer nerves and muscles of the neck, and in these cases there was usually a recurrence. These were sometimes local and quite benign, and the patient might live for many years, the type tending to become more and more sarcomatous with each recurrence.

DR. R. T. FRANK said in regard to the second case, that as far as he could see, Dr. Ewing had spoken of one type of cell which was epithelial in character; that is, resembled chorioma. The cystic growth with high cuboidal epithelium would represent ectoderm. He had understood Dr. Ewing to say that this was a teratoma with but one layer developed.

DR. EWING said that he had regarded it as a tridermal structure. He could not feel certain that the cells were really choriomatous, and therefore could not say that they were ectodermal structures.

As there seemed to be some disagreement still among the members of the committee as to the diagnosis of the second case the President again referred the matter to them for further study and report.

* * * * *

At the meeting of the Society held on January 12, 1910, the Committee on Microscopy reported as follows:

The first tumor submitted by Dr. Martland at the November meeting of the New York Pathological Society is a chondroendothelioma or mixed tumor of the submaxillary gland.

The ovarian tumor is a teratoma of the ovary with carcinomatous changes.

(Signed) CHARLES NORRIS
F. C. WOOD
J. EWING, Chairman.

THREE UNUSUAL TUMORS.
SARCOMA OF THE STOMACH, ENCHONDROMA OF THE VERTEBRA, AND CARCINOMA OF THE KIDNEY.

ELI MOSCHCOWITZ, M.D.

Dr. Eli Moschcowitz presented three tumors, rather ordinary in type, but of interest because of their unusual locations.

The first was a tumor of the stomach removed from a woman fifty-eight years of age. The history was incomplete, as the patient was practically moribund upon admission to Beth Israel Hospital. She had, however, been treated for ulcer of the stomach at the German Hospital about a month previously. She had remained there for two weeks, and had then been at home for two weeks, when she was suddenly seized with violent pain, and showed typical symptoms of general peritonitis. The diagnosis of perforated gastric ulcer was made, but at operation none could be found. At autopsy, a tumor, the size and shape of a potato, was found situated at the greater curvature of the stomach, near the esophagus, high up under the left lobe of the diaphragm, adherent to the diaphragm on one side and resting on the spleen on the other. The tumor was pedunculated. In the stomach there was a large ulcer about the size of a penny, which led into a long cavity within the tumor. On section, the surface of the growth was white, interspersed with numerous hemorrhagic areas. On microscopical examination, the tumor proved to be a typical spindle cell sarcoma. No metastases were found.

The second case was one of enchondroma of the vertebra, removed from a patient, forty-eight years of age, who was admitted to the Beth Israel Hospital on June 15. About eleven years before his left lower extremity had begun to feel heavy; this heaviness slowly increased for a time, and then, according to the patient, the symptoms entirely disappeared. Some time later the feeling of heaviness returned, and the right lower extremity also became affected; numbness, stiffness, and spasticity developed. He also had pains about the abdomen. During

the three weeks before admission the pains had been excruciating. On physical examination the spastic gait was very pronounced, more especially in the right leg. There were some areas of general hyperesthesia. The sensations of heat and cold were much impaired. Knee jerks were exaggerated. Wassermann and Noguchi tests were negative. At operation a tumor about the size of a pecan nut was found springing from the posterior aspect of the ninth dorsal vertebra, somewhat to the left of the median line. The tumor was smooth and very hard. The patient died two months after the operation, with all the classical symptoms of transverse myelitis. On microscopical examination the tumor proved to be an enchondroma, showing areas of softening and areas of calcification. The spinal cord was compressed to such an extent that practically nothing but dura was left. On microscopical examination the ascending tracts were degenerated above the tumor, the descending below.

The third specimen was removed from a man, fifty years of age, who five years previously had noticed lesions on both legs, which were diagnosed as multiple hemorrhagic idiopathic sarcomata of Kaposi. For a year and a half, he had suffered also from attacks of pain in the right kidney, with occasional hematuria. The urine was full of pus, but no tubercle bacilli could be found. Nephrectomy was performed, and the patient died about a month later. The kidney showed a large pedunculated papillary mass springing from the upper part of the pelvis, about the size of a walnut. On section through the pedicle, infiltration of the kidney by tumor tissue could be seen to a depth of about an inch and a half. The markings of the remaining part of the kidney were practically obliterated. The cut section was smooth and white in color. The capsule was adherent; and the fatty capsule was also adherent. The pelvis of the kidney presented a large number of large tubercles with cheesy contents. There was no ulceration. Microscopically, the tumor was a papillary carcinoma. The kidney was infiltrated throughout with round cells; the tubercles of the pelvis showed the typical changes of tuberculosis. At the autopsy, an old tuberculosis of both apices was found; but there were no metastatic growths.

Discussion:

DR. CHARLES NORRIS asked Dr. Moschcowitz upon what grounds he based his diagnosis in the first case, and how he excluded a primary sarcoma of the perigastric or peripancreatic lymph nodes. Could he exclude a secondary metastatic tumor? The ulcer in this case might have been secondary; the tumor might have ulcerated through the coats of the stomach.

DR. MOSCHCOWITZ said that microscopically the tumor was not of the type usually derived from the lymph nodes. It was a typical spindle cell sarcoma. That the tumor was primary was shown by the fact that at autopsy no other tumor was found.

DR. HORST OERTEL said that he felt rather doubtful as to the sarcomatous character of the growth in this first case. He had not yet seen the microscopic sections, but in the gross it seemed to him to present a good many features which were against such a diagnosis. The growth was apparently well limited; it did not seem to infiltrate the stomach at all, projecting rather to the outside, but without involving the surrounding structures; and no metastases were present; points which were unusual in a primary sarcoma of the stomach. Dr. Oertel asked how Dr. Moschcowitz excluded a possible origin from another source, and whether he was absolutely certain that the tissues represented a sarcoma.

DR. MOSCHCOWITZ said that his diagnosis was based upon the miscroscopical appearances, which were those of typical spindle cell sarcoma. There was in the slides nothing to indicate gumma. As far as the character of the tumor went, it conformed to many tumors of the stomach which had previously been described in the laboratory. Some of these tumors were diffuse, while others were pendulous. As regarded the possibility of a lymphatic origin, this could not be absolutely excluded, but microscopically the tumor was not of the type usually found arising from the lymph glands. The tumor was in intimate relation with the stomach; there was no line of cleavage or any other sign to show that the growth arose from any other organ than the stomach.

Dr. Oertel asked whether the tumor infiltrated the mucous membrane, or whether it had shown any tendency at all toward infiltration.

Dr. Moschcowitz said that the mucous membrane was not infiltrated except at the site of the ulceration; and that the tumor had shown no tendency whatever to infiltrate, except the wall of the stomach.

Dr. A. M. Pappenheimer recalled having performed an autopsy upon an undoubted case of primary sarcoma of the stomach. The subject was a male, forty-two years old. The stomach was occupied by a tumor mass the size of a child's head, presenting within the cavity of the organ, and taking its origin from the fundus. The tumor weighed over three kilos. The growth infiltrated the upper pole of the spleen and the diaphragm at one point; elsewhere the peritoneum was smooth. The internal surface was covered with greenish slough. The tumor consisted of homogeneous, yellowish white tissue, which in places had broken down to form cysts filled with clear fluid. There were several large metastases in the liver, but none of the regional lymph nodes were involved. Microscopically, the tumor consisted of long, slender, tapering cells, arranged in loose bundles and whorls. The nuclei were elongated and frequently had squared ends. The cells stained like smooth muscle fibers, and no intracellular connective tissue fibrils could be demonstrated. In many places the cells were separated by abundant homogeneous ground substance taking a faint eosin stain. The tumor was considered to be a leiomyosarcoma.

Dr. Oertel said that he was still unwilling, on the evidence so far presented, to accept this case as one of primary sarcoma of the stomach. (After examing the microscopic slides, Dr. Oertel took the tumor to be a myoma of the stomach.)

FOUR DIFFERENT CASES ILLUSTRATING RUPTURE OF THE AORTA.

A. K. DETWILLER, M.D.

The following cases of rupture of the aorta seem to be of interest, not only from the standpoint of pathological anatomy, but also as regards the question of how far syphilis enters in as an essential factor in the production of all such cases. While syphilis is usually classed as one of the causes of arterio- or athero-sclerosis, it is frequently associated with a more specific inflammation of arterial disease. Here its effects on the aorta seem to be mainly of the nature of periarteritis and of mesaortitis. These specially definite syphilitic types generally show a somewhat localized distribution. Certain parts of the aorta, most commonly the arch, seem to be particularly susceptible to this process, while the rest of the vessel may, as far as gross appearances go, appear healthy.

In fibrous aortitis, the inner surface of the vessels is characteristically scarred and often puckered with narrow, linear furrows, sometimes showing little pits from which stellate lines radiate. Commonly, there is a very characteristic translucency, due to areas of localized atrophy. Hard patches, sometimes almost cartilaginous in appearance, and of grayish white color, are seen forming round, oval, or irregular areas, more or less raised above the surface. There may also occur white patches of recently formed connective tissue with possibly an entire absence of the ordinary yellowish raised nodules and calcified plaques, so generally seen in atheroma.

Microscopically, syphilitic aortitis begins, according to the present prevalent belief, in the form of granulomatous infiltrations of the adventitia and media along the course of the individual vasa vasorum. These vessels proliferate with the production of newly formed capillaries and other associated evidences of syphilitic inflammations. Accompanying this infiltration, a localized atrophy and final disappearance of the normal elements of the middle coat occur. The elastic tissue layers, especially,

are subject to the most striking and, at the same time, most important change, consisting of a disintegration, fibrillation, and eventual disappearance in those areas where inflammatory cell infiltration has taken place. The destruction of the elastic laminæ must have a very considerable influence in the production of aneurysmal dilatation and in rupture of the aorta.

The first case occurred in a Spaniard, forty-eight years of age, who was admitted to the skin ward, at the City Hospital, on account of multiple small tertiary ulcerations of the scalp of six weeks' duration. He gave a history of hard chancre, seventeen years previously, with a subsequent development of extensive skin eruption. The clinical diagnosis was tertiary syphilis. He was put on potassium iodide and hypodermic injections of salicylate of mercury. Physical examination revealed nothing except punched out ulcers of the scalp and typical syphilitic scars on the legs. The patient was afebrile and felt well; in fact, he had asked to be discharged. He died very suddenly, nine days after admission to the hospital, from a severe hemorrhage, blood flowing freely from his mouth and nose.

The autopsy showed a considerable number of white, translucent looking scars confined to the first and second portions of the arch of the aorta; the thoracic and abdominal parts being well preserved. There was an annular, punched out ulcer communicating with the trachea at the point where they cross each other. The ulcer was circular, its edges somewhat undermined and its base adherent to the subjacent trachea. The perforation was four mm. in diameter, extending from the base of the aortic ulcer into the trachea and through this the fatal hemorrhage had occurred. There was no special aneurysmal dilatation of the arch; this at its widest part measuring only 8.5 cm. in its internal circumference. The stomach was found to be nearly filled with semi-clotted blood and the lungs were in a state of acute emphysema and filled with aspirated blood. The liver showed a gumma and numerous typical syphilitic scars. There was no smooth atrophy of the base of the tongue; this being an example of the extent of the importance which can be attached to the ab-

sence of an often-quoted, most reliable sign of syphilitic disease.

The next case occurred in a large, well developed man, fifty-nine years of age, who previously had been apparently in perfect health. No history was obtainable in this case so that the question of syphilis could not be determined. He died very suddenly in bed, during the night.

At autopsy, the pericardium was found filled with blood. The first portion of the arch of the aorta showed a slight general dilatation. Along its right margin, just at the point where the blood stream is thrown on its new course, while the aorta is still within the pericardial sac, there were two small, slit-like apertures. They were situated in the longitudinal axis of the vessel, being about three mm. long and separated by thin, fibrous tissue, two mm. broad. Through these apertures communicating with the interior of the aorta, the hemorrhage into the pericardium was derived.

The interior of the first and second portion of the arch was thickened and showed a few whitish scars with occasional grayish white, raised nodules. The rest of the aorta was unusually well preserved. There was a long split, three cm. in length, extending through the intima and media, at the base of which were the apertures through the adventitia on the outer surface of the vessel, as before described.

The third case was that of a woman, fifty-seven years of age, who had presented a clinical diagnosis of asthma and cardiac insufficiency. She died very suddenly while in bed at night. At autopsy, a right hemothorax was found. The aorta showed extensive atheromatous changes throughout. The calcareous plaques were not particularly numerous. There were numerous yellowish raised patches. Occasionally there could be seen yellowish, somewhat translucent looking scars, sometimes with radiating linear furrows. In the lower portion of the thoracic aorta, one cm. above the opening in the diaphragm, a slit-like aperture situated in the long axis of the vessel and communicating with the posterior mediastinum and right pleural cavity, was found. This rent went completely through the intima and media

to the adventitia, where a small dissecting aneurysm had formed before the rupture occurred.

A fourth case, showing a rather unique condition of the aorta, occurred in a German, forty years of age. He entered the hospital, complaining of ulcer on the right leg, of eight weeks' duration. This healed rapidly under anti-syphilitic treatment. He denied syphilis, but had suffered from gonorrhea eight times; besides the evidence of syphilis existing in his typical scars on the legs, he also presented a characteristic sinking of the bridge of the nose. He eventually developed, following urethral in-strumentation, an acute vegetative endocarditis with a general septicemia, from which he died.

At autopsy, there was discovered an acute staphylococcal endocarditis with acute degenerative changes throughout the body. There was also an extremely enlarged spleen, weight 1,250 gms., and the liver was in a state of subacute cirrhosis. Just above the aortic valve, were three small, circular, punched out, deep ulcers, about three mm. broad, and extending through to the adventitia of the aorta. One of these ulcers led to a small aneurysm about one cm. in length and closely attached to the pulmonary artery, bulging somewhat on its inner wall.

These sharply punched out ulcers were very much like those which were found in the first case. Of course, the presence of an endocarditis in this case complicates it, as there is a possibility that some adherent vegetations might have caused these excava-tions.

Microscopically, the process causing these ulcers was evi-dently a chronic one; the elastic laminæ of the aorta were ab-ruptly destroyed at the margins. As in the first case, no spirochetes were found in the ulcers of the aorta.

In conclusion, difficult as it is to draw very definite deduc-tions in these cases, I think that there is some ground for stating that syphilis must be a very large factor in the production of conditions leading to rupture of the aorta and also of aneurysmal dilatation. Some of the cases I have demonstrated have shown ulcerations of the aorta practically independent of ordinary

atheroma and occurring in extremely syphilitic subjects. In deciding how far such rupture of the aorta can occur, independently of syphilis, I would invite the discussion of the Society.

Discussion :

DR. OERTEL pointed out as a promising field for discussion, the question of the relation of syphilitic disease of the arteries to general arteriosclerosis, and particularly to rupture of the aorta. Of particular interest to him was the fourth case reported by Dr. Detwiller, in which the small aneurysmal perforations were complicated by an ulcerative endocarditis of the aortic valve. The remainder of the aorta appeared to be in pretty good condition. The question arose whether these small, blind, and apparently healed perforations were the result of a very localized syphilitic disease or of inflammatory ulcerations.

DR. JAMES EWING said that his idea about syphilitic aortitis was something which showed traces of the *Spirochaete pallida*. In the absence of this sign he felt it was hardly worth while sticking too closely to old teachings. It seemed to him, however, that the evidence in favor of the syphilitic nature of most of the lesions presented by Dr. Detwiller, and of the punched-out ulcers was rather strong. He thought there was great need of working over the whole subject of constitutional syphilis from the point of view of the demonstration of *Spirochaete pallida*, because these organisms have been found well preserved in very old lesions. The demonstration of even fragments of the *Spirochaete pallida* was of considerable importance, and could be made use of in many fields where no systematic attempt had thus far been made to demonstrate them. The appearance of the fragmented *Spirochaete pallida* was very characteristic. Feeling as he did, Dr. Ewing had been disappointed to learn that Dr. Detwiller had not succeeded in finding traces of the *Spirochaete pallida* in these lesions. Dr. Ewing was not disposed to think that all the diseases of the aorta which he had been taught many years ago were unquestionably syphilitic were really of that origin. Again, he did not now believe that many of the characteristic lesions of the kidney, such as had been believed to be absolutely certain signs of syphilis, were really due to this disease.

PARATYPHOID CHOLECYSTITIS.

RUSSELL S. CECIL, M.D.

The striking similarity which exists between typhoid and paratyphoid fever holds true not only for their mode of onset and clinical manifestations, but also as regards the character of the complications encountered. Secondary paratyphoid infecttions of the bones, joints, testicle, middle ear, and bladder have all been reported; while, according to Lorraine Smith, intestinal hemorrhages occur in 5 per cent. of all cases.

The frequency of typhoid cholecystitis would, therefore, warrant the expectation of meeting often with gall-bladder diseases in paratyphoid fever. While such may be true, I have been able to collect from the literature only six authentic cases of paratyphoid cholecystitis. Lorey reported a case of paratyphoid cholecystitis, Type B, in 1908, and claimed that he could find in the literature no other cases of that type which were entirely free from objections.

The case of paratyphoid cholecystitis which I am about to report falls under the Type A group, and is especially interesting in that the patient gave no history of a previous attack of typhoid or paratyphoid fever.

L. C.; female, age twenty-five, married; admitted November 23, 1908, to the first surgical division of the Presbyterian Hospital, complaining of abdominal pain, nausea, and vomiting. Family history negative. Personal history negative. Measles in childhood. No other acute illness. No history of typhoid or paratyphoid fever. Present history: Two years ago patient was suddenly taken with severe colicky pains in gall-bladder region. Attack was accompanied with vomiting, fever, and slight jaundice. About one year later, patient had another attack, similar to the first. Since then she has been subject to frequent attacks. For the last three weeks she has been constantly ill. Pain is very severe and radiates to back. Nausea, headache, and fever constant.

Physical examination: Patient is fairly well nourished, but

looks ill. Chest negative. Abdomen is soft except in upper right
quadrant, where there is some resistance. In the region of the
gall-bladder there is a pear-shaped mass, moving with respira-
tion, and slightly tender. Temperature, 101.5°; leucocytes,
12,600. Urine shows bile. Clinical diagnosis: Cholelithiasis.

On November 25 a cholecystectomy was performed by Dr.
Eliot. At the operation, the omentum was found firmly adherent
to the gall-bladder. Wall of gall-bladder was thickened; mucosa
was swollen. Gall-bladder contained greenish, semiviscid bile,
and numberless small stones. The bile ducts were patent. An
abscess containing two ounces of pus was found near the fora-
men of Winslow. Microscopically, the mucus membrane of the
gall-bladder is partially absent, and the other coats are densely
infiltrated with polymorphonuclear leucocytes and lymphoid
cells. Smears from the gall-bladder mucosa show many poly-
morphonuclear leucocytes, and small Gram negative bacilli. Cul-
tures from the bile, and also from the interior of one of the
stones, give a pure growth of an actively motile, Gram negative
bacillus. On agar, this organism forms small greyish-white
translucent colonies. Litmus milk is slightly acidified, but there
is no coagulation or liquefaction after two weeks' growth.
Neither blood serum nor gelatin is liquefied. In Dunham's
peptone solution, no indol is produced. Broth becomes turbid,
but no pellicle is formed. Glucose broth, 1 per cent. is fermented,
with the production of a small amount of gas; saccharose broth
is free from gas. In lactose broth there is at first no gas, but
at the end of a week there is a minute bubble. In mannit broth
a small bubble after several days. One cubic centimeter of the
twenty-four hour broth culture, when injected intraperitoneally,
killed a guinea-pig in less than twenty-four hours. Agglutination
tests with patient's serum were carried out with a number of
organisms. The typhoid bacillus was not agglutinated, even by
high concentrations of the patient's serum The colon bacillus
was not agglutinated at a dilution of 1-20.: The patient's own
organism was agglutinated at a dilution of 1-200. Two other
strains of paratyphoid bacillus, Type A, were agglutinated at a

dilution of 1-50, both microscopically and macroscopically. Two strains of Bacillus paratyphosus, Type B, were not agglutinated at a dilution of 1-20.

On December 12, seventeen days after the operation, the patient's feces were examined for paratyphoid bacilli. Endo's medium was used for the plates. No paratyphoid bacilli were found.

In this case we have the picture of a typical chronic cholecystitis, produced by an organism which corresponds in every way with Kayser's paratyphoid A bacillus. This case bears a striking resemblance to the one reported by Blumenthal. His patient, a woman forty-six years old, gave no history of typhoid or paratyphoid fever. At the operation there were found thirty-six gall-stones, cultures from which gave a pure growth of the paratyphoid A bacillus. The agglutination test was positive at a dilution of 1-300.

In 1903, Pratt reported a case of cholelithiasis in a girl, eighteen years old, who was operated on four years after an attack of fever diagnosed as typhoid. Cultures from the gall-bladder and from the stones gave a pure growth of the paratyphoid B bacillus. The patient's serum agglutinated her own organism, but had no effect on the typhoid bacillus.

Lorey's case is similar to Pratt's. A young man, twenty-two years old, giving a history of typhoid fever two years previous to his attacks of gall-stone colic, underwent an operation. Four stones were found in the gall-bladder. Cultures from the gall-bladder mucosa showed a pure growth of the paratyphoid B bacillus. The patient's serum agglutinated his own organism, as did also the serum from two cases of paratyphoid fever.

Zimmer has recently reported a case of paratyphoid cholecystitis which was diagnosed from a bacteriological examination of the feces. The paratyphoid B bacillus was isolated. This organism was agglutinated by the serum from a case of paratyphoid fever, but the patient's serum failed to agglutinate his own organism. There was no surgical or post-mortem examination in this case.

Forster and Kayser examined the bile of one hundred and forty-eight cadavers for bacteria, and found the paratyphoid bacillus only once, and that in a case of diabetes mellitus. The gall-bladder contained two stones. The bile gave a pure culture of the paratyphoid B bacillus, but cultures from the interior of the stones were sterile. In this case there was no history of typhoid or paratyphoid fever. The identity of the bacillus was established by "the usual cultural and immunity reactions."

In addition to these five cases of paratyphoid cholecystitis, several observers have found paratyphoid bacilli in gall-bladders that showed no pathological changes. Dr. Libman, as far back as 1902, isolated the paratyphoid bacillus from the gall-bladder in a case of paratyphoid fever which was operated on for suspected gall-bladder disease. The gall-bladder was distended with thick, dark bile which could not be pressed out. After the operation intense jaundice developed and the patient died on the following day. At the autopsy, however, the gall-bladder and bile ducts showed no changes.

Luchsch has reported a case of paratyphoid fever that came to autopsy. Cultures from the bile showed the organism, but there were no inflammatory changes in the gall-bladder.

Discussion :

Dr. E. Libman said that the case to which Dr. Cecil had referred was considered before operation to be a case of cholecystitis. At the time of the operation there was slight jaundice, high temperature, and marked tenderness in the region of the gall-bladder. At the operation the gall-bladder was found distended with bile; the wall was absolutely normal, both macroscopically and microscopically. There were parenchymatous degeneration of the liver and a deposit of fibrin on the surface near the gall-bladder. This recent perihepatitis had caused the symptoms which suggested an involvement of the gall-bladder.

As regarded the method of elimination of bacteria through the bile, Dr. Libman stated that he had observed one case which

suggested that sometimes there may be such an elimination of bacteria from the liver through the bile without the bacteria first entering the general circulation. He cited a case of suppurative pylephlebitis due to streptococci, in which although the blood cultures were negative, streptococci were found in the gallbladder. A case of paratyphoid cholecystitis had recently been observed in Mt. Sinai Hospital, and this case had been studied by Dr. Rosensohn, the pathological interne, who would state his findings.

DR. ROSENSOHN said that at Dr. Libman's suggestion he had looked through the records of the laboratory from April, 1904, up to the present time, and had found records of 257 bacteriological examinations of the contents of gall-bladders. In nine of these cases typhoid bacilli were found in the bile, and in one case the paratyphoid bacillus was found. The patient from whose gall-bladder the paratyphoid organism was isolated was a woman forty years of age. Some fifteen years before her recent illness she had been in bed two weeks with a disease which was diagnosed as typhoid fever, and which was very mild in character. Three or four years after that time she began to suffer from attacks of jaundice and pain in the region of the gall-bladder, being perfectly well between the attacks. During the past summer the patient was seized with intense pain in the region of the gall-bladder, and developed high temperature and marked jaundice. She was treated by Dr. Manges who referred her to Dr. A. A. Berg for operation. The gall-bladder was found very markedly distended, being about the size of a fist. The bile which was aspirated was described by Dr. Berg as being of peculiar color, resembling methylene blue. Dr. Berg said that he had never before seen exactly that color in a fluid obtained from the gall-bladder. The paratyphoid organism which was isolated from the bile was typical in its character. Milk was only slightly acidified; there was no secondary alkalinity. Unlike Dr. Cecil's organism no gas was produced in lactose. The mucous membrane of the gall-bladder was thickened; no material was sent to the laboratory for microscopical examina-

tion. The gall-bladder, common duct, cystic duct, and some of the hepatic ducts were filled with calculi. The gall-bladder was removed and the patient made an uneventful recovery. The serum of the patient had no agglutinating effect upon the typhoid bacillus, but agglutinated the paratyphoid organism which was isolated from the bile in dilutions up to 1-100.

Dr. Charles Norris was under the impression that in the course of ordinary routine examinations of bile in his laboratory, they had had several cases from which paratyphoid organisms had been cultivated; at least two or three in the last four years. It would probably be determined through extensive routine examinations in time, that the paratyphoid bacillus, while not found so frequently as the colon, was present in a large number of cases. As had been shown, it was a more or less constant inhabitant of the upper portion of the gut. In autopsies on cases of meat poisoning due to paratyphoid-like organisms and also in typhoid fever, the organisms were always found in large numbers in the bile. Dr. Cecil had said that his organism after a considerable number of days produced only a bubble of gas in mannit and caused only slight acidification of milk. In Dr. Norris' experience with these organisms, paratyphoid and paracolon bacilli produced abundant gas in mannit, and gave only a primary and temporary acidification of milk. If the milk were left in the incubator there was a strong alkali production. He would rather question whether the organism which Dr. Cecil had described was really a paratyphoid bacillus.

Dr. Cecil, referring to the point brought up by Dr. Norris, the action of the bacillus on milk, said that he had observed this carefully, as he was familiar with the usual action on milk. In several tests there was only faint acidity produced with no change after a few days. Recently he had re-tested the bacillus, and had found that it still formed a very faint acid reaction which did not become alkaline. The agglutination reactions were so marked that it was impossible to feel any doubt as to the nature of the organism.

SUDDEN DEATH IN CONSTITUTIONAL SYPHILIS DUE TO EXTENSIVE SYPHILITIC LARYNGITIS.

A. K. DETWILLER, M.D.

The specimen presented was removed from a comparatively young man, twenty-seven years of age, who gave a definite specific history, stating that his primary lesion had occurred in October, 1906. This was followed by a secondary eruption and throat symptoms. He had been under constant treatment since that time. Eighteen months after the primary lesion he was admitted to the City Hospital with very extensive tertiary lesions. He had four deep ulcerations on his forehead and considerable destruction of the cartilaginous portions of his nose. He was put on antisyphilitic treatment, several hundred grains of iodide being given daily. After a year of such treatment he was discharged, but was still employed about the hospital as an orderly. For the last few months he was troubled with severe specific laryngitis, which began with husky voice, ending in complete loss of phonation. He also began to suffer with attacks of dyspnea which occurred at special times, as when he was required to do some heavy lifting, or go up a flight of stairs. During one of these so-called "asthmatic" attacks brought on by running up a flight of stairs, he suddenly became cyanotic and died in a short time. The physician who saw him thought the cause of death was acute dilatation of the heart or possibly ruptured aneurysm. At autopsy there was nothing to account for his sudden death except a nearly complete stenosis of the lower half of the larynx. In addition there was found extensive destruction of the cartilaginous portions of the nose. On one side of the face was a large shiny scar which began at the angle of the mouth and reached to the temple; there were also several scars over the forehead. The base of the tongue showed a rather hypertrophic condition of the papillæ, some of which were greatly swollen. The epiglottis was almost completely ulcerated away, only a small stump remaining. There was marked thickening of the arytenoepiglottic folds due to the extensive infiltration. At the time

of autopsy some edema was present. Examination of the under surface of the larynx showed that the cellular infiltration extended down to the fifth ring in the trachea. A cross section just beneath the vocal cords showed a very striking stenosis, which in the unhardened specimen had been almost complete. The tissue was very dense and firm.

The liver presented numerous gummata, some on the surface, and some in the interior of the organ. Some areas were caseous and others were quite hard. The abdominal aorta was comparatively well preserved, smooth and glistening throughout, except that along its posterior wall there were some fine light linear markings, possibly a part of his constitutional disease, namely, a beginning syphilitic aortitis. A series of lantern slides was presented showing the lesions in question very clearly.

THE MARESCH METHOD FOR STAINING TISSUE SECTIONS.*

WILLIAM H. WOGLOM, M.D.

In 1905, Maresch[1] published a modification of the stain of Bielschowsky and Pollak[2] for neuro-fibrillæ, which he recommended highly for the demonstration of fine connective fibers, such as one finds in the liver and in the lymph nodes, and for the study of the same fibers in tumors. These fibers appear in the sections an intense black. His technique is, in short, as follows:

Formalin fixed tissues are embedded in paraffin. After cutting, they are floated out on warm 2 per cent. silver nitrate solution, in which they remain for twelve to twenty-four hours.

*Read by Dr. F. C. Wood.
[1]*Centralbl. f. allg. Pathol.*, xvi, 1905, 641.
[2]*Neurol. Centralbl.*, 1904, 387.

After a thorough washing in distilled water, they are transferred to the following solution, which must be freshly prepared:

2 per cent. silver nitrate solution..........20 c.c.
40 per cent. sodium hydrate solution........ 3 drops
        Ammonia......Enough to dissolve the precipitate

After two to thirty minutes in this solution, the sections are washed in distilled water, and then reduced in 20 per cent. formalin. Reduction takes place almost instantly. After washing in distilled water. the sections are transferred to an acid gold toning bath:

Distilled water ....10 c.c.
1 per cent. aqueous sol. gold chloride...... 3 drops
Glacial acetic acid.................... 3 drops

In this they remain for about ten minutes, at the end of which period unreduced silver can be removed by immersion for one-half minute in a 5 per cent. solution of hyposulphite of soda. The sections are then floated out on warm water and mounted on glycerin-albumin covered slides. After the sections are dry the paraffin is removed with xylol, and the sections mounted in damar.

Celloidin sections may be used, in which case it is well to dissolve out the celloidin before impregnation. The technique for frozen sections is essentially the same as that for paraffin sections.

In 1909, Kuro, at the meeting of the Deutsche pathologische Gesellschaft,[3] described the differentiation between sarcoma and carcinoma by means of this stain. In carcinoma, fine fibrils are never found between the cells as they are in sarcoma. These fibrils are stained an intense black, while the ordinary collagen fibers take on a more brownish tone.

Stimulated by the illustrations accompanying this article, we tried the method on a variety of tissues. Fibrin and elastic tissue do not take on the intense black which is assumed by the connective tissue fibrils. but are rather brownish in their tone.

[3]*Verhandl.* 1909, 386.

The method affords a striking and beautiful demonstration of even the very finest fibrils in the liver, in the lymph nodes, and in malignant growths. Considerable difficulty was experienced in impregnating frozen sections, and as there seemed to be no advantage in their use the attempt was given up, and thin paraffin sections were used exclusively. As there was a great deal of shrinkage in the sections which had been for twelve to twenty-four hours in silver nitrate, and as the whole section was often too black to be of any real use, it seemed advantageous to shorten the time. It was found that five minutes in silver nitrate was enough to demonstrate the fibrils, while at the same time shrinkage was to a great extent eliminated, and the details of the nuclei and cell bodies became much more evident. Whether sections prepared by thus shortening the time will be as permanent as the others, it is impossible to say. The only other change which has been made has been to fasten the sections to the slides before staining is begun. Sections from which the paraffin has been removed before staining seem to stain, on the whole, more regularly than those which are carried through the process with the paraffin still present. There is great danger, however, of their coming off the slide, although the use of a thin film of celloidin would probably obviate this difficulty.

A considerable series of tumors have been stained by this method and show a variety of interesting appearances. In the carcinomata one finds black fibrils which pass around small nests of epithelial cells but do not penetrate between them. In the true sarcomata each cell is generally paralleled by fine fibrils. The cells of the mixed tumors of the salivary glands do not usually show fibrils between them. Certain of the tumors coming from pigmented moles have shown connective tissue between the cells; others have shown none. The results with certain other obscure forms of malignant new growths have been somewhat doubtful. Occasionally one will see the periphery of the cells stained, giving the appearance of an intercellular fibril network. Probably, however, this is a staining of the intercellular cement substance. On the whole, the silver method is of considerable practical value

in aiding in the differentiation between carcinoma and sarcoma; but there is not infrequently much difficulty in getting suitable stains, and the results are quite inconstant as to the depth and extent of the fibril stain. While, therefore, it is a useful adjuvant to our diagnostic methods, it is by no means a certain clue to tumor nomenclature.

THROMBOSIS OF THE LEFT JUGULAR AND SUBCLAVIAN VEINS.

H. LE B. PETERS, M.D.

This specimen of thrombosis of the left jugular and subclavian veins, with agonal extension to the right ventricle in mitral stenosis was from a woman, thirty-eight years of age, who was admitted to Dr. N. B. Potter's service at the City Hospital on October 26, 1909, complaining of "shortness of breath, weakness, and palpitation of the heart." Her symptoms dated back to April, 1909, when she had apparently suffered from a typical attack of acute rheumatic fever. During that time, she had considerable dyspnea, especially upon slight exertion, palpitation, a hacking cough, some cardiac distress, and marked engorgement and pulsation in the veins of her neck. These symptoms improved somewhat under treatment in Bellevue Hospital, only to recur shortly after her discharge. The only point of importance in her previous history was repeated attacks of rheumatism, extending over a period of twenty years.

On admission, she was found to have typical signs of mitral stenosis, with a failing compensation, a large heart, presystolic thrill, presystolic and systolic murmur at apex, an irregular pulse, and a marked distention of the veins of the neck with positive venous pulse. On December 2, about three weeks before death, the patient complained of pain in the left side of the neck and in the left axilla. The upper part of the left arm was

swollen and tender; and what was taken for the left subclavian vein was hard, tender, and hot. This acute condition lasted only about two days and then subsided. Subsequently, the lower part of the left jugular vein was felt to be hard, as was also the left axillary vein. Her heart condition became gradually worse and she developed a general edema. The edema was much more marked in the left than in the right arm.

The temperature, from November 20 until her death, on December 23, 1909, was irregular, ranging from 98° to 102°. The blood count on December 1, one day before the thrombosis was first noted, was 3,384,000 red blood cells, 60 per cent. hemoglobin, 14,000 leucocytes.

Autopsy: The heart was large, weighing over 700 gms. The mitral orifice admitted only the tip of one finger. The other valves were apparently healthy. From the junction of the left jugular and subclavian veins, extending 20 to 25 cm. through the subclavian, axillary and brachial veins, and about 12 cm. up the left jugular vein, was a thrombus (of the mixed variety) firmly attached to the vessel walls and apparently completely obstructing the lumen of the veins. From the junction of the left jugular and subclavian veins, a white thrombus of smaller caliber extended through the left innominate and superior vena cava, ending in a large, bulb-like projection in the right auricle. This was quite firmly attached near the point of division of the left innominate, but was otherwise not adherent to the walls of the vessel nor in the right auricle. The intima of the superior vena cava, not involved in the thrombosis, was smooth and glistening, as were also the veins of the right side, and the brachial vein distal to the region involved in the thrombosis.

Microscopical Examination: A section of vein from apparently the oldest part of the thrombosis showed considerable thickening and some inflammatory change, but it was impossible to determine from the section whether the vascular change was primary or subsequent to the thrombus formation. The thrombus itself was undergoing considerable organization.

The mixed thrombus was probably of three weeks' dura-

tion, forming at the time of her symptoms; while the other, on account of its character and its slight adhesion to the vessel wall, appeared of more recent and probably agonal formation.

The case is interesting on account of its comparative infrequency—a relatively small number of cases of peripheral thrombosis in cardiac disease having been reported.

Hanot and Kahn, in reporting a similar case, could find only five others in the French literature. Welch, in 1900, was able to collect in all a report of twenty-seven cases, while since that time Desquiens, in 1906, has collected thirty-nine cases.

Of Welch's twenty-seven cases, twenty-three attacked the veins of the neck, upper extremity, or both. Of the twenty-three cases, fourteen were confined to the left side, seven were bilateral and in only two were the veins of the right side exclusively affected. Of Desquiens' thirty-nine cases, thirty-seven involved some branch of the superior vena cava. The comparative frequency with which the upper extremity is involved in the condition is rather remarkable, when we consider that venous thrombosis from all causes is said by Bouchet to be fifty times more frequent in the lower than in the upper extremity.

According to Welch "The associated valvular disease of the heart is almost invariably mitral—stenosis, with or without incompetence, taking the lead."

The cause of thrombosis in cardiac disease is still a matter of discussion. Hanot and Kahn attribute it to the cachectic state during the last stages of cardiac diseases. Poynton, in discussing three cases reported by Cheadle and Lees in 1898[1], refers the thrombosis to a rheumatic phlebitis, although bacteriological examination was negative. Two of these cases showed a mitral stenosis, and the third an acute mitral endocarditis of rheumatic origin.

Schmidt considers the thrombosis due simply to stasis, while Letulle and Gatay[2] hold to rheumatic phlebitis as the cause.

[1] *Lancet*, July, 1898.
[2] Gatay, La phlebite rhumatismale. *Gaz. hebd. de méd.* Feb., 1896.

Welch thinks that the most probable cause is a terminal infection, and that the localization is due to the pressure, direct or indirect, of the left auricle and engorged pulmonary vessels on the left innominate vein.

Discussion:

Dr. Charles Norris asked whether there had been any infection of the left arm in this case.

Dr. Peters said that there had not.

OBSERVATIONS ON THE ANTIFORMIN METHOD FOR THE DETECTION OF TUBERCLE BACILLI AND THE VALUE OF THE HERMAN STAIN.

CHARLES KRUMWIEDE, JR., M.D., AND LOUISA P. BLACKBURN.

(*From the Research Laboratory, Department of Health, New York.*)

Numerous efforts have been made to perfect a method by which sputum, negative for tubercle bacilli by direct smear, can be fluidified so that subsequent sedimentation, by gravity or centrifuge, will concentrate the bacilli, if present, and render detection easier. No satisfactory method had been evolved till Uhlenhuth[1], in 1908, advised the use of antiformin, a hypochlorite solution with sodium hydrate added, as the solvent agent. While testing its disinfectant and solvent powers, he found that not only were nearly all bacteria quickly killed and dissolved by it, but numerous organic substances were attacked. On trying its effect on tuberculous sputum, this was found to be quickly fluidified; but within limits neither the staining properties nor the viability of the tubercle bacilli were affected. In general, the following method has been used, the variations being in time of action and strength of antiformin used.

The sputum is mixed with antiformin so that the total

strength of the latter is 15 per cent. After vigorous shaking, the mixture is allowed to stand until completely fluidified, which will depend on the character of the sputum. The specific gravity of the mixture is then reduced, if necessary, by adding water or alcohol to facilitate sedimentation and the fluid centrifuged for one-half hour. The supernatant fluid is then poured off and the sediment shaken up in water and recentrifuged. This washing is necessary, as otherwise the material does not spread well on the slide, and staining is interfered with. After pouring off the water, smears are made from the sediment and stained. The results, as reported by Uhlenhuth, Hüne,[2] Thilenius,[3] Seeman,[4] and Meyer,[5] have been very good. The last reported 14 per cent. positive results with negative sputa, in some instances the sputum for twenty hours being used and only three or four bacilli found.

Previous to the introduction of antiformin, Lange and Nitsche[6] had found that if a hydrocarbon be added to fluidified sputum and thoroughly shaken, as the hydrocarbon rises again it carries up the tubercle bacilli which will be found at the junction of the two fluids when the emulsion clears. They suggested the use of ligroin and advised this method as a substitute for centrifuging. The clearing of the emulsion and rise of the ligroin are aided by standing the mixture in the incubator or in a water bath at 60° C. Smears are made by taking repeated loopfuls of material, at the junction of the two fluids, and placing them on the same spot on a warmed slide. Practically nothing stains except tubercle bacilli.

Haserodt,[7] and later Bernhardt[8] and Jacobson[9] applied the ligroin procedure to the antiformin treated sputum with good results. Haserodt used both methods on 300 negative sputa with 7 per cent. positive results. On the ground of comparative results with twenty sputa prepared by mixing different samples, he comes to the conclusion that the ligroin method is more favorable than centrifuging.

We have examined the following specimens of sputa to judge of the practicability of the antiformin method as a rou-

tine method of diagnosis and incidentally to compare the crystal-violet (Herman)[10] and carbol-fuchsin stains.

Twenty-eight sputa considered negative by the diagnostic laboratory and five sputa containing varying numbers of tubercle bacilli were examined. The method consisted in diluting anti-formin with two parts of water, adding an equal volume to the sputum, shaking a few times and allowing the sputum antiformin mixture to stand over night. The resulting homogeneous mixture was then treated as already described, using the centrifuge method.

The carbol-fuchsin stained smears were decolorized and counterstained in Pappenheim's solution; the crystal-violet stained smears were decolorized in 10 per cent. nitric acid, rinsed in alcohol, and counterstained in Bismark brown. Where smears are said to have been restained with carbol-fuchsin, the heating was prolonged to about three minutes, the slide decolorized as in the crystal-violet method, and simply dipped in methylene blue (1 per cent.) to render the counterstain very light.

In all cases the duplicate slides were made from the same material, carrying it from slide to slide with careful mixing, rendering them as uniform as possible. We have considered these slides as identical, which naturally cannot be the case, but the final average would rule out accidental variations in the individual slides.

Of the twenty-eight negative sputa examined two were positive, on less than five minutes' search, in slides made directly from the sputum. Of the remaining twenty-six, four were positive in the sediment alone; that is, 15 per cent. positive results with the antiformin.

The first two sputa were also negative with us, after painstaking search of carbol-fuchsin preparations. In one case the sediment was also negative with the carbol-fuchsin stain, but bacilli very numerous with the crystal-violet stain. All the carbol-fuchsin slides were then restained and the bacilli easily found, though even then the preparations were not quite as good as those stained with crystal violet. In other words, if these ex-

aminations had been controlled with crystal-violet stain, a few minutes' search would have shown them positive.

Of the four specimens which were positive in the sediment alone, the carbol-fuchsin stain failed, though the crystal-violet stain revealed bacilli. On restaining the carbol-fuchsin slides, however, bacilli were found in three of the specimens, though decidedly fewer in number. The results in the fourth specimen were probably accidental, due to difference in number of bacilli on the individual slides. This leaves no doubt as to which is the better stain.

Five control specimens were examined to confirm the above findings and to see the relative merits of slight modifications of technique.

In three specimens the concentration was over one hundred fold in the sediment. Comparative counts showed more bacilli in the sputum stained with crystal violet, and in using the sediment the carbol-fuchsin slides were very poor and required restaining. The use of alcohol to reduce the specific gravity of the antiformin sputum mixture was tried and gave better sedimentation and clearer and better stained preparations.

The ligroin method was tried both on positive and negative sputa. The results in the few instances we have tried it have not been as good as with the centrifuge method. It failed where the centrifuge method was positive.

The amount of sputum used in the centrifuge method has been from three to seven c.c.

From the comparative work done we conclude that every sputum should be examined with the crystal-violet stain, if negative with carbol-fuchsin. Further, that as a routine procedure one volume of the antiformin-sputum mixture to one or two volumes of alcohol, depending on the character of the mixture, will give the best results, and in the ordinary centrifuge tube will give sufficient sediment for two slides, which, if stained with crystal violet and found negative, can be considered negative. Larger volumes of sputum would give better results probably, but more smears would be required and the time consumed would be pro-

hibitive except in special instances. The guinea-pig would be cheaper if slower.

As to the difficulty with the carbol-fuchsin stain, possibly two factors are at work, the decolorizing action of methylene blue, and overstaining and blotting out of fuchsin stained bacilli. Very light staining with methylene blue, just sufficient to clear the field and give a contrast, should be done. If other organisms are to be observed a second preparation had better be made.

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[9]JACOBSON: Comptes Rend. Soc. de Biologie. Tome LXVII, No. 32.
[10]HERMAN: Ann. Inst. Pasteur. Tome XXII, No. 1.
(See also CAAN, Cent. f. Bakt. Orig. Bd. XLIX, s. 637, for comparison of newer staining methods.)

Discussion:

DR. HANS ZINSSER asked Dr. Krumwiede what results he had had in the cultivation of the bacilli after treatment with anti-formin. This method had been used in a few cases at St. Luke's Hospital laboratory, with excellent results in morphological study alone, where the bacilli were found after centrifugaliza-tion in enormous numbers. Although not done systematically, two or three attempts to cultivate these bacilli had failed. It was a question whether the failures were due to the fact that the bacilli were not washed long enough after the treatment, or to the fact that they had been exposed too long; or whether the cultivation of the bacilli was not so easy as Uhlenhuth had stated in his first communication.

DR. E. LIBMAN said that he had had an interne working

with the antiformin method at Mt. Sinai for a couple of months,
so far with very excellent success. He thought that one great
advantage would be apparent in animal inoculation work. In-
oculated animals were often lost because of infection with other
organisms. Here there was a method available for eliminating
the contaminating organisms before inoculation. Dr. Libman
also said that while visiting at Saranac Lake last summer, Dr.
Brown had shown him a number of successful cultures made
after the antiformin method. He had apparently had no diffi-
culty in cultivating the organisms.

Dr. F. C. Wood said that he had used the Herman method
in staining sections with great satisfaction. At least, one could
find, in presumably tuberculous tissue, bacilli which were not
demonstrable by the ordinary carbol-fuchsin tissue stains. He
had not used it, however, in staining sputa, as he had always con-
sidered the carbol-fuchsin stain with differentiation in Pappen-
heim's solution quite satisfactory.

Dr. Richard M. Pearce said that he had had no experi-
ence with this method. He thought, however, that it was a mis-
take to exploit in a scientific paper any preparation under a pro-
prietary name. He understood that this substance had been
known to chemists for years; and in these days of crusades
against proprietary articles it seemed a mistake to exploit this
preparation in this way.

Dr. A. F. Hess said that he had given to the pharmacists
at the Board of Health laboratory the exact prescription for this
substance according to Uhlenhuth's formula, but the results ob-
tained were not at all the same. Evidently the solution was quite
different. Possibly the preparation could be made, but their at-
tempt had been a failure.

Dr. Krumwiede, in answering Dr. Zinsser, said that he
had failed also in the attempt to make cultures, though he had
not given much time to the matter. The antiformin seemed to
affect the viability on culture media, even though animal inocu-
lations might be positive. Uhlenhuth says not to expose the bacilli
to antiformin any longer than necessary. He advises contrifugal-

izing immediately after the sputum is fluidified. As regarded
the proprietary phase of the subject, Dr. Krumwiede said that
he, too, had tried to compound the formula which was given to
him, but that he could not get the same results. Uhlenhuth claims
that a further advantage is the keeping quality of antiformin.

A CASE OF SEPSIS DUE TO BACILLUS PYOCYANEUS.

ALFRED F HESS, M.D.

(Research Laboratory, Department of Health, New York City.)

It is not so many years ago that there was doubt as to the
occurrence of a primary sepsis due to *Bacillus pyocyaneus*.
During the past few years, however, several cases of this nature
have been reported, where this organism has been cultivated
from the blood during life, as well as recovered from the various
organs after death. The cases are not so numerous, perhaps, as
to make it inappropriate to report in brief an additional instance
which has come to my attention.

The patient was a girl, almost three years of age, one of
three children of healthy parents. She had always been well un-
til four days previous to the time when I first saw her. The
mother stated that during these days the child had suffered from
a moderate diarrhea, with slimy stools accompanied by malaise
and fever. The case was considered by me to be one of indi-
gestion, and castor oil and a fluid diet were prescribed. Two
days later the child was again seen by me, but no unusual symp-
toms were noted. She did not look as well; the temperature was
101° F.

On the following day some petechial spots were noted on
the palpebral conjunctiva, as well as on the body, and, as the
patient's general condition was worse, a blood culture was taken.
Three cubic centimeters of blood were obtained from the vein at
the elbow, under strict aseptic precautions, and injected into

flasks of broth and glucose broth.   In these a pure culture of *B. pyocyaneus* developed.   One-half cubic centimeter of a forty-eight-hour broth culture of this organism was fatal to guinea-pigs when inoculated intraperitoneally.

The further clinical history is as follows: The child-lived six days from the date of the taking of the blood culture. She grew rapidly weaker; large subcutaneous hemorrhages developed upon the trunk and the extremities, some containing pus; the diarrhea persisted, five to eight stools being voided in the course of the day.   The stools had a peculiar fetid odor, and were composed largely of pus and mucus tinged with blood.   The temperature ranged between 99° and 104°.   The day previous to the fatal exitus, the right ear showed a discharge of thick yellow pus.   Physical examination of the child disclosed nothing additional, excepting enlargement of the spleen and more especially of the liver.

As has been mentioned, *B. pyocyaneus* was cultivated from the blood during life.   In addition, it was isolated from the urine, from the aural discharge, and from one of the skin lesions which contained bloody pus.   It was also cultivated from the heart's blood which was aspirated post mortem.   No further autopsy was allowed.

We seem to have here undoubtedly a case of general infection due to *B. pyocyaneus* as the primary and sole invader of the system.   The portal of entry appears to have been the intestine, so far as we can judge from the early symptoms.   The nature of the invading organism could not have been diagnosed nor, I believe, even suspected from the clinical course, as the pus in the aural discharge, in the skin lesions, and in the stools did not present the characteristic color.   The etiology of the infection remains obscure.

Discussion:

DR. E. LIBMAN considered this case one of the most interesting cases of general pyocyaneus infection which had been reported.   The fact that the discharge did not have the usual yel-

low color was particularly interesting. In infections of the middle ear by *B. pyocyaneus* the first pus is usually white and does not have the characteristic odor; but after discharging for a time, the typical color is usually developed; that is, as soon as the external air gains access to the ear the real color of the pus is produced. Dr. Libman had had three cases of general infection by *B. pyocyaneus,* all of which were interesting. The first case was in a patient who had had an attack of acute febrile icterus. In his blood *Staphylococcus pyogenes aureus* was found. The patient improved and was fairly well for about a week, when he again developed severe symptoms, and *B. pyocyaneus* was found in the blood. After death the same bacillus was found in the heart's blood. *Staphylococcus aureus* was found in an abscess of the vastus externus muscle. The infection by *B. pyocyaneus* was a secondary one. The second case was simply an ante-mortem infection. The third case had occurred within the last few months, and was one of the very few definite cases in which recovery followed. The patient entered the hospital with a severe cystitis which had persisted for some time. After instrumentation he developed chills and a temperature. *Bacterium coli* was found in the blood; a few days later both *Bacterium coli* and *B. pyocyaneus* were found. Cultures of the urine also showed both. A third blood culture showed *B. pyocyaneus* alone. The patient made a complete recovery.

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HENRY J. NICHOLS,
Captain, Medical Corps, U. S. A.

The discovery of the cause of syphilis by Schaudinn had an important sequel for tropical medicine in the discovery of the cause of yaws by Castellani in the same year, 1905. Castellani[1] says that in February of that year while examining smears from a case of yaws at Colombo in Ceylon, he found two

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kinds of spirochetes, one fairly large and one almost invisible
with a strong Leishman stain. He paid little attention to them
at the time, however, because he also found numbers of bacteria
and undetermined oval bodies. You will recall that Schaudinn[2]
found living spirochetes from a syphilitic lesion on March 3,
1905, that he stained these organisms wtih Giemsa's stain and
that the report of Schaudinn and Hoffman appeared in May,
1905. After reading this report Castellani again took up the
examination, also using Giemsa's stain, and again in a number
of cases found the same tenuous spirochete which he considered
morphologically identical with *Spirochæta pallida* and named
Spirochæta pertenuis or *pallidula*. He sent slides to Schaudinn,
who found besides two kinds of large spirochetes, one which he
too considered morphologically identical with *Sp. pallida*. Cas-
tellani made a tentative report in June and also in November,
1905. Meanwhile Wellman[3] had at about the same time found
in one case spirochetes, which he at first mistook for spirilla of
relapsing fever, in serum from a yaw; no such organisms, how-
ever, were found in three other cases of yaws.

Castellani inoculated three monkeys, and in one, after six-
teen days at the site of inoculation, a yaw-like lesion developed
which repeatedly showed *Treponema pertenuis*. Later he de-
veloped the subject more fully.

Castellani's observations have been fully confirmed and ex-
tended in various parts of the world, particularly in Java and
the Philippine Islands, so that it is now as certain that yaws is
due to a spirochete as that syphilis is.

The finding of an organism in yaws which both Schaudinn
and Castellani considered morphologically identical with *Spiro-
chæta pallida* naturally raised the old question about the identity
of the two diseases. As you doubtless recall, Hutchinson[4] has
a theory that yaws is the original form of syphilis which has
become modified by passage through the Caucasian race. To
Hutchinson and his followers the finding of the spirochetes
seemed to clinch the matter; but without reviewing all the evi-
dence at present it may be said that everyone who has worked

with the disease recently believes that yaws is not syphilis; as Castellani puts it, yaws is not syphilis any more than leprosy is tuberculosis.

The infectious nature of yaws has been known for a long time. Manson[5] says that the planters in the West Indies had yaw houses and other repressive measures to keep the disease under. Paulet[6], in 1848, inoculated seventeen negroes, all of whom developed the disease in twelve to twenty days; in thirteen cases the disease developed at the site of inoculation, in the other four cases it was generalized. Charlouis[7], a military surgeon in Batavia, in 1881 autoinoculated four cases and three developed additional yaws. He inoculated thirty-two Chinese prisoners and twenty-eight became infected. He then took a case of yaws in a Malay, explained the dangers of syphilis and proposed inoculation; the man agreed, and he produced a chancre on the chest, followed by a secondary eruption and glandular enlargement. Yaws and syphilis have been observed clinically in the same person at the same time in several instances.

Yaws has been studied experimentally in monkeys by Castellani[1], by Baerman and Halberstädter[8] of Neisser's expedition to Java, and by Ashburn and Craig[9] of the U. S. Army Board for the Study of Tropical Diseases as they exist in the Philippine Islands. As a result of their work we can formulate the following statements:

1.   Yaws can be transmitted from man to monkey; from monkey to monkey, and from one part of the body to another; the serum from the yaws, the blood, the lymphatic glands, the spleen pulp and bone marrow may be infectious; the spinal fluid is not infectious; filtered fluids and extracts are not infectious.

2.   In the monkey as in man the lesions are usually confined to the site of inoculation or the immediate region by autoinoculation; a general eruption may, however, occur.

3.   Syphilis can be inoculated in an animal with yaws and vice versa. Castellani claims that he could demonstrate specific antigen and antibodies for yaws distinct from those of syphilis.

Histologically a yaw consists in an overgrowth and down-

growth of the epithelial layers of the skin with edema and cellular infiltration of the corium, which together make a rounded mass of oozing papillæ. The treponema are found only among the degenerated epithelial downgrowths; there is no perivascular infiltration, there are no giant cells and there is very little reaction of the fixed connective tissue cells.

Although Schaudinn and Castellani found no morphological difference between *Treponema pertenuis* and *pallida*, Prowazek[10] believes that there are certain general differences between them. Major Russell[11] has also studied the two organisms and agrees with Prowazek. These differences which can be best shown in the slides are as follows:

Treponema pertenuis is slightly thicker and less rigid; the twists are not so regular; there is more tendency for the ends to curl up; the forms with longitudinal divisions are more numerous.

As a summary we may say that yaws is usually a localized disease of the skin and is spread by autoinoculation; general infection with general eruption may, however, occur. The following is a brief clinical description based on observations controlled by experiments.

Yaws is common on the west coast of Africa, in the West Indies and in the islands of the far East, from Ceylon to Samoa. Manson[5] believes it probable that it was brought to the West Indies from Africa by the slaves. It is described by travelers as far back as 1567 as the pox.

There is but one lesion, the yaw or raspberry-like growth on the skin. Initial lesions and sequelæ, such as ulcers, have been described by the older writers, but these views have not been substantiated. It is essentially a disease of childhood; in some places in the Philippines, as among the Moros who live in a communal system, practically every child has it, like measles among us. Daniels[5] says that in Fiji children who do not take the disease are inoculated by their parents, who regard an attack of yaws as more or less necessary and wholesome.

In children then we find these "fungoid excrescences" cov-

ered by a yellow crust of dried serum in various parts of the
body, usually following autoinoculation from some other yaw,
but occasionally occurring in definite crops. There may be a
general glandular involvement, but there are no definite con-
stitutional symptoms. The disease lasts a few months and grad-
ually disappears.

In adults there may be pains in the joints and bones and
loss of weight. Many of the cases in adults come from children
by direct contact; for example, I have seen a mother with a
yaw on her flank from carrying astride her hip her child whose
buttocks were affected; again, a yaw on the breast from suckling
a child whose lips were covered with yaws; and several grand-
fathers with a few yaws on the neck or head from carrying
children. The same kind of contact infection probably occurs
from child to child, although it is possible that flies and other
insects may carry the organisms. To illustrate contact infection:
several of us a short time ago made a medical survey of a typical
Filipino town and found all the cases of yaws in groups. For
example, in one house, two cases, child, age three, and grand-
father, age seventy, with history of a third; in the next house,
one case, child, age two; in the next house two cases, child, age
two, mother, age twenty-five; and no other cases anywhere in
the neighborhood. Sexual infection is very rare indeed; the
only case at all suggestive was that of a prostitute with a yaw
on the labium.

The evidence against the identity of the disease with syph-
ilis is as follows:

1. Geographical distribution; yaws is confined to certain
tropical regions; it exists where there is no syphilis, and has also
died out while syphilis remained.

2. Yaws and syphilis may occur in the same person, and
there is no immunity from one disease to the other.

3. The lesions in yaws are always the same, not pleo-
morphic.

4. The lesions of yaws affect principally the epithelial, not
the connective tissue.
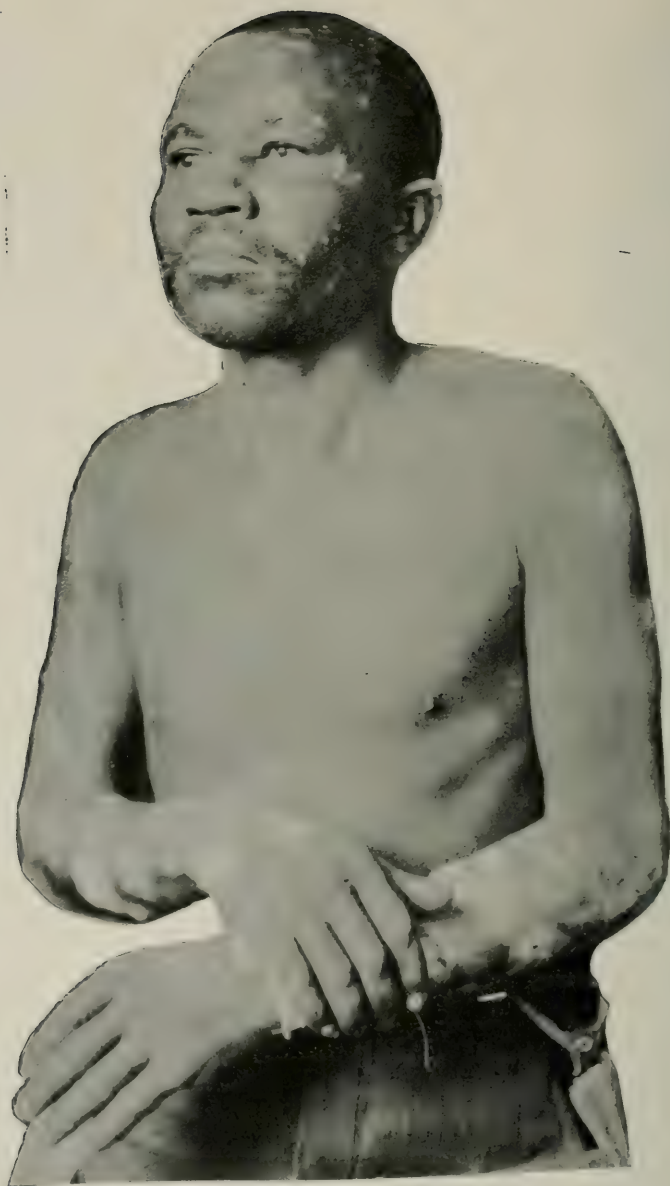
Yaws in colored soldier; showing second crop of lesions, smooth white patches of healed yaws and circular outline of granulation in still active yaws.

5. Yaws is principally a disease of children; but is neither hereditary nor congenital.

6. The lesions are extragenital and sexual transmission is practically unknown.

7. Constitutional symptoms are not the rule in yaws.

8. The treponemas may differ morphologically.

The occasion for the present paper is the occurrence of a well marked case of yaws in a colored soldier who returned from the Philippines last summer.

J. F.: Corporal, 10th Cavalry; age forty years. Family history is good; there is no evidence of syphilis.

Patient had measles and mumps in childhood, gonorrhea in 1907; emphatically denies any other venereal disease. He has been in the army eighteen years and was in the Philippine Islands in 1901-3 and 1907-9. He left Manila on May 15, 1909, in good condition; was exposed to venereal disease on May 12, in a small town near Fort McKinley, where he was stationed. He has seen yaws among native children, but did not come in contact with any cases as far as he knows.

The transport came home by the Suez Canal, arriving about July 25. While on board, about June 1, he developed pains in the chest and later in the joints, which became so severe that he was taken into the hospital for the last three weeks of the trip. The transport touched at Singapore, Colombo, and Aden; but there is no poetical fitness in the stop at Ceylon, as the men were not allowed ashore. The patient went ashore only once at Aden for about two hours, and had nothing to do with any of its people. After reaching New York, on July 25, he went to Fort Ethan Allen, Vermont, and entered the hospital immediately with the same vague rheumatic pains. On August 10, he noticed a small lump or pimple on his left cheek, and three days later a general eruption of the same kind on his back, chest, arms, legs, hands and feet. The lesion started as a papule, increased gradually, and became covered with a yellow crust which covered an oozing granulation. The medical officers in charge suspected yaws and gave him potassium iodide and

yellow iodide of mercury, under which his pains improved and
the lesions gradually dried up, until at the end of about six weeks
he was entirely well. About four days later, October 2, a second
crop of the same sort of lesions appeared on his face, arms and
legs.

On December 9, he was transferred to Governor's Island by
direction of the Surgeon-General for observation by Capt. J. F.
Siler, who is giving a course in Tropical Medicine at the Post-
Graduate School.

I saw the patient in December, and he was then recovering
from a typical attack of yaws. Most of the yaws were nearly
gone, but he still had several typical fungoid excrescences with
a yellow crust. The papillæ were rather drier and more fibrous
than is usual. He had a general glandular involvement and
complained of pains and swelling in the ankles and knees and loss
of weight. On two examinations treponemas were found in the
serum from the yaws, by the dark field microscope.

He had been treated with mercury and potassium iodide;
this treatment was changed to atoxyl, and in a few weeks his
skin was entirely clear, except for white patches marking the
site of the previous eruption of yaws. About a week ago a third
crop of yaws broke out on his arms and legs; these are small and
are already retrogressing. He is again on atoxyl.

On December 17, I took the patient to the Rockefeller Insti-
tute and excised a piece of one of the yaws, which Dr. Flexner
rubbed into a slightly abraded surface over a rhesus monkey's
eyebrow. The primary abrasion healed completely, but twenty
days later a scaliness was noted along the eyebrow, and in a few
days a well marked papular ridge developed. This ridge broke
down into an ulcer which discharged serum copiously. Trepo-
nemas have been repeatedly found in the serum from this lesion,
usually few in numbers, but on one day in abundance. The other
eyebrow was inoculated from the first one on January 3, a
lesion appeared on February 2. Inoculations have also been
made in rabbits' testicles.

The serum from the patient does not give the complement

Papular ridge with ulceration and copious discharge of serum. Incubation, twenty days. *Treponema pertenuis* found repeatedly.

fixation reaction for syphilis. The monkey's serum is also nega-
tive in this respect. The patient's blood and urine show nothing
noteworthy.

If the infection occurred in the Philippine Islands, the in-
cubation period is eighty-six days, which is very long, although
in one of the experimental cases in monkeys the incubation period
was ninety-six days; however, it is possible that the rheumatic
pains which began about two weeks after leaving the islands
were the beginning of a systemic infection which did not break
out until late. This is one of the rarer cases of general eruption;
all of the yaws are of practically the same age. Beside this case,
I have seen one case of yaws in a white soldier who contracted
the disease in Balangiga, Samar, where a number of children
were affected. He too had a general eruption with several
recurrences.

The increase of travel between the Tropics and the United
States as a result of our expansion has raised the question of the
importation of various diseases, but in the case of most parasites
there seems little to fear. A few years ago considerable interest
was aroused in England about the possibility of the introduction
of *Schistosomum hæmatobium* by discharged soldiers from
Egypt and South Africa; but no cases have ever been found
arising in England. The possibility of infecting our own Tropics
has also come up. In the Philippine Islands I saw a white sol-
dier with a bilharzia colitis contracted in Porto Rico. This man
was sent back to San Francisco. In the Philippine Islands I have
also seen a Porto Rican and a colored soldier just arrived with
Filaria nocturna, and *Strongyloides*. *Schistosomum hæmatobium*
is unknown in the Philippine Islands, although we do have
Schistosomum japanicum; the other two parasites are already
there.

In the Philippine Islands I have also seen a colored man
with ainhum, from Jamaica. It is not rare to have cases of
typhoid fever develop on transports going to the islands, and
some medical men have claimed that typhoid was introduced
into the tropics in recent years, but I doubt this statement as

well as the statement that amebic dysentery in the United States is due to imported cases, but this is another story. At any rate, the danger of the spread of yaws seems remote in a fairly clean and well ordered community in the temperate zone.

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Discussion.

DR. JAY F. SCHAMBERG wished to express his indebtedness to Dr. Nichols for the opportunity of seeing this very rare and interesting dermatosis. The chief point of interest would be the differentiation of such cases from syphilis. In the patient demonstrated, the absence of eruption on the trunk with profuse involvement of the face and extremities would argue against syphilis.

DR. BOLESLAW LAPOWSKI referred to the occurrence of syphilitic papules in the folds of skin about the nose and ear, which he considered characteristic of the disease, and asked Dr. Nichols whether he had noticed papules of this kind in yaws. So far as his reading went he had never seen any mention made of papules here. He also asked Dr. Nichols how he could be sure that the spirochete which he had described was the cause of the disease. He thought there was at present no proof that

the organism was the etiological factor and that it might be wiser to say only that it was present. The organisms had not yet been satisfactorily described; even Schaudinn had said that he recognized them by instinct, and Dr. Nichols had said that he could not always distinguish the spirochetes of yaws and syphilis. Proof that the spirochete was the cause of syphilis would not be forthcoming until the presence of the organism in an embryo was demonstrated.

DR. NICHOLS could not add anything very definite about the localization of the papules in the folds, as had been spoken of. In some cases one found a yaw on the lip which gradually spread up and covered the side of the nose. About the ear he could say nothing from memory. In cases of general eruption, the particular localization did not seem to have much to do with it. In regard to the treponema being the cause of yaws, Dr. Nichols had simply expressed the opinion that yaws was due to a spirochete as certainly as syphilis was.

A CASE OF DELHI BOIL.

JAMES EWING, M.D.

The case which I have to present occurred in the Cornell Dispensary in the class of Dr. James C. Johnston. The patient was a Sicilian, twenty-one years of age, who had been in this country for four years. Three years ago he fell downstairs and hit his forehead on a step, and some time thereafter noticed a small lump or swelling in the skin, which has persisted until now. At the time of examination, this induration in the skin extended over an area about 2 cm. broad, and on palpation the tissues were found to be thickened to a depth of about 0.5 cm. The epithelium was slightly eroded over this area, which was light-colored, and might be described as a large maculo-papule. There was no ulceration. The elevation was about 0.3 cm. at the high-

est point, and was irregular. The border was also more or less irregular.. The consistence was distinctly less than that of a chancre; otherwise it had somewhat the same appearance. The lesion was evidently of considerable dermatological interest, and as the diagnosis was not clear a small piece of tissue was excised by Dr. Johnston for microscopical examination. As a matter of routine many pieces of tissue from various cases in the dispensary practice are examined in the laboratory, and when a section from this lesion came under my eye I hesitated whether to call it infectious granuloma of unknown origin or an endothelioma because of the large number of endothelioid cells. The large cells, however, showed peculiar granulations; and on examination with the oil immersion lens, bodies were found which proved to be the parasites of Delhi boil. There was an infiltration beneath the epithelium consisting of large vacuolated clear cells with pale staining nuclei and minute sharp granules which varied greatly in number. There was no infiltration about the blood vessels and no necrosis; but there was evident degeneration of the phagocytic cells. Minute study of the sections failed to reveal anything of particular histological interest, except to confirm the original impression that the disease was Delhi boil. The most successful staining was done by the old-fashioned Nocht-Romanowsky method. On account of some successful cultivations obtained by Nicolle[1] of such parasites, an attempt was made to secure cultures from this case, and an incision was made through the skin, and the blood and fluid were squeezed out and transferred to several tubes of Nicolle's medium. This medium consists of agar 14.0, sea salt 6.0, water 900, to which is added one-third volume of defibrinated rabbit blood. On this medium Nicolle, as well as Rach and Zarff[2], secured luxuriant cultures. No satisfactory growth was obtained in this case, however, and a positive result cannot be reported. The morphology of the bodies in the cells, however, seems to be identical with those in the case of Delhi boil reported by Wright, and

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[1]*Centralbl. f. Bakteriol.*, 1906, xlii, 488.
[2]*Deutsch. Arch. f. klin. Med.*, 1909, xcvi, 387.

also with the case of kala-azar reported by Marchand, material
from which was given to me by Marchand in Leipzig some years
ago. I am not prepared to place this lesion in its dermatological
series, nor to say that it is a true Delhi boil. It is an infection
of the skin showing bodies which are practically identical in
appearance with those of kala-azar, and are also identical in
appearance with the bodies described by Wright. Possibly they
are a little smaller than the bodies seen in either of these cases.

It is interesting to note that this man was in this country
for two years before any sign of trouble occurred in the skin;
and that the lesion has progressed for two years since the trauma,
the relation of which to the lesion is of course very doubtful.
No parasites could be found in the blood; the spleen was not
enlarged; and there were no signs of any other lesion in the
body.

"GRAIN ITCH," A NEW DISEASE IN THIS COUNTRY.

JAY F. SCHAMBERG, M.D.

In the late spring of 1901, there appeared in Philadelphia
and its vicinity an unfamiliar eruptive disease which attracted
the interest and attention of dermatologists. It was recognized
that the disease was new. At that time, having observed a dozen
or more cases and photographed several, Dr. Schamberg pub-
lished a description of the affection in the *Philadelphia Medical
Journal* of July 6. Since 1901, this same affection has appeared
in greater or less degree from the month of May to the month
of October, in Philadelphia and its vicinity. In 1909, at about
the same season, an unusual prevalence of this disease was no-
ticed, and an outbreak occurring among sailors on a private yacht
lying in the Delaware River attracted the attention of the city
and Federal health authorities. Dr. Joseph Goldberger was
delegated by the Surgeon-General of the Public Health and
Marine Hospital Service to investigate the outbreak. As Dr.

Schamberg had had some experience with the previous epi-
demics, and was studying the prevailing one, he and Dr. Gold-
berger conducted the inquiry jointly.

Upon investigation it was found that there had recently
been received on this particular yacht a consignment of new
straw mattresses, and that only those sailors who had slept on
these new mattresses contracted the disease. It was also learned
that other outbreaks had occurred on several other boats lying
along the river, and on investigation the same conditions as to
the receipt and use of these straw mattresses were found. Infor-
mation was received from various sources and some seventy
cases were investigated in the city of Philadelphia occurring in
various residences and boarding houses. In every instance it
was possible to connect the appearance of the eruption with the
use of a new straw mattress. Several of these mattresses were
secured, and Dr. Goldberger placed his bare arm and shoulder
in contact with the straw for one hour. At the end of sixteen
hours the characteristic eruption developed on the arm, shoulder
and chest. The straw from the mattresses was then sifted
through a very fine sieve, and on careful examination it was
possible to detect slight motion. The moving particles were
transferred to a slide and microscopically proved to be minute
mites, scarcely visible to the naked eye, though the motion was
visible. These specimens were submitted to Mr. Nathan Banks
of the Department of Agriculture, who identified them as allied
to or identical with *Pediculoides ventricosus*.

Dr. Goldberger then applied some of the siftings in a Petri
dish to the axilla of a volunteer, and produced the lesions in a
short time. Chloroformized siftings, however, failed to evoke
the development of an eruption.

All of the mattresses were traced to four manufacturers,
and it was found that the one common source of the infected
supply was Salem County, New Jersey; one of the manufac-
turers securing all of his straw from this place.

The lesion produced by this mite was quite characteristic
and differed from lesions of other diseases. With the onset of

the disease, there is apt to be some constitutional disturbance. Some patients develop fever of 100° to 102°F., with the usual febrile accompaniments. There is sometimes enlargement of the glands, and occasionally chilliness, nausea, and even vomiting may occur. The characteristic lesion of the disease is a hive-like efflorescence on the skin, in the middle of which there is a minute vesicle, extremely small, often only 0.5 mm. in diameter, sometimes 2 or 3 mm. The vesicle rapidly becomes pustular. As a result of the intense itching, the patient scratches the skin and the vesicles are converted into small blood crusts. The eruption is usually extensive and involves chiefly the trunk and extremities, seldom, however, extending below the elbows or knees; the hands and feet are practically always free. The face may show scant lesions. The lesions vary greatly in size, are of a warm rose tint, and slightly raised. The intense itching which is usually present leads to scratching, and the latter to the appearance of excoriations and at times pyogenic complications. One of the patients was suspected of having smallpox, although a greater resemblance to chickenpox is usually presented. In some instances the lesions are much larger than in others; there appears to be an inverse proportion between the number of lesions and their individual size. In some cases, the disease is apt to be confounded with hives, and in others with common "itch"; the absence of the eruption on the hands, and the character of the lesion, would help to eliminate scabies.

Blood examinations were made on the twenty sailors interned at St. Agnes' Hospital; these showed a moderate leucocytosis, the average number in the twenty cases being about 8,500, although some cases had 10,000 and 11,000. Four days later examination showed an average decrease of about 1,000. The eosinophiles at the first examination averaged 5 per cent.; though some patients had 9 or 10 per cent. Four days later the average was reduced to 2.5 per cent. No special cells were found, and the other blood elements were normal. Careful urinary examinations were made, and of the twenty patients, three showed albuminuria; this is doubtless analogous with the albuminuria found in scabies.

The cause being known, the disease was readily cured. Before the cause was discovered, the disease persisted for weeks because the patients continued to sleep on the infected mattresses.

While it was at first thought that the disease was localized to Philadelphia, evidence was later obtained showing that it was much more widespread. In both Indiana and Ohio it has occurred to a considerable extent for the past few years. Farmers gathering straw have been so badly affected that they and their employees have refused to go near the infected straw. In Pittsburg, in 1898, some porters who had carried sacks of barley from a car to a wagon were all badly attacked, and the horses themselves were affected. Dr. Rawles has recently published a series of cases in which farmers and others were attacked in small towns in Indiana. In the August number of the *British Dermatological Journal*, Dr. Willis of Bristol reported an outbreak of an identical disease among some twenty porters who had carried sacks of barley. He made a careful study, but erroneously came to the conclusion that the urticaria was due to vegetable hairs.

The parasite is not new. It was first mentioned by Newport in 1850, and in 1878 was given the name *Pediculoides ventricosus*. A number of outbreaks of an eruptive disease in Hungary and Russia are recorded occurring as long ago as 1849, resulting from contact with wheat and barley. At that time a parasite allied to or identical with *Pediculoides ventricosus* was found.

Microscopical examination of the lesion shows that pathologically it is distinctly an urticaria. One sees an epidermal vesiculation with destruction of the epithelial cells. In the corium there is dense infiltration of round cells and of polymorphonuclear leucocytes. Large numbers of mast cells are present. There is no vertical cleavage of the epidermis to indicate that a puncture has taken place. The parasite evidently does not burrow into the skin.

The mite is predatory and parasitic on soft bodied insects. It has been found on the larvæ of wasps; Prof. F. M. Webster, of the Agricultural Department, has for a number of years been

interested in this mite, because it is predatory on the grain-destroying insects. *Pediculoides ventricosus* is of a straw color, long oval shape, with mandibles which act as lancets or needles; the legs are quite characteristic. The mite in the nymph stage has only three sets of legs; later it acquires a fourth pair. When gravid, the abdomen of the parasite swells to an enormous size, twenty to one hundred times the rest of the body.

As has been said, this small mite is of considerable economic importance since the wheat-straw worm, on which it is parasitic, is the great enemy of wheat in the fields of the West, and occasions great havoc. East of the Mississippi, an allied species, the joint worm, does equal damage. In addition to these two grain-destroying parasites, the pediculoides preys upon the grain moth, which attacks the wheat in the barn.

Pediculoides ventricosus finds its nourishment in the larvæ of these insects and destroys them, thus conserving the crops.

In all probability we may look forward to an increasing prevalence of this disease. It appears to be spreading; recently outbreaks have been reported in Italy. No name had hitherto been applied to the disease, and it seemed to Dr. Schamberg wise to give it some designation. He had thought that the name "Grain Itch" would be suitable as a popular appellation and "Acaro-Dermatitis Urticarioides" as a scientific one.

Discussion.

DR. JOHN A. FORDYCE thought that the Society was to be congratulated on the opportunity of listening to this very carefully worked up presentation. It was not often that one had the good fortune to describe a new disease. It had occurred to him that some of the cases described as urticaria in immigrants by Dr. J. C. White several years ago might be the same disease. These cases occurred in newly arrived immigrants in this country, who quite possibly had been infected on the steamer coming over. Dr. Fordyce had seen a number of such cases himself, which were classed as urticarias due to change of diet or possibly as psychical in nature.

Dr. Boleslaw Lapowski asked Dr. Schamberg whether he would be able without seeing the parasite under the microscope to make a diagnosis. Would a person not familiar with the disease be able to make a differential diagnosis between this new disease and other urticarias? Could Dr. Schamberg tell why certain straw was infected, while other straw was not?

Dr. Schamberg said that he surmised that Dr. Fordyce's thought was probably correct; some of the cases described as "immigrant itch" probably were cases of this character. He had seen a number of such cases in past years and the resemblance was suggestive. The eruption here, he thought, to anyone who had once seen a well developed case, was absolutely characteristic, provided it was seen before scratching. There was an extensive eruption of an urticarial nature, but most of the wheals were surmounted by a minute vesicle. Unless the source of the infection were destroyed, this eruption continued for a long period of time: it did not run the short course of the usual urticaria. It sometimes might be confounded with the itch, but the absence of lesions on the hands would readily distinguish it. The straw that contains these grain-destroying parasites offers a nidus for the mite also. The United States Government had devoted considerable research to methods of prevention of infection of straw by these grain-destroying parasites. One of the best methods is that of rotation of crops, since the crop of one year is apt to become infected by that of the preceding year.

THE TRACHOMA BODIES IN SMEAR AND SECTION, WITH DEMONSTRATIONS.*

HIDEYO NOGUCHI, M.D., AND MARTIN COHEN, M.D.

PART I.—*Microscopical Studies.* (*Dr. Noguchi.*)

Interest in the question of the etiology of trachoma was suddenly aroused following the announcement of Halberstaedter and v. Prowazek[1] of their discovery of characteristic inclusions in the conjunctival epithelia of a Javanese youth suffering from trachoma. They found these cell inclusions in the smears stained with the Giemsa solution. The original descriptions of the finding may be quoted here.

"Die blauen amorphen Massen der Einschlüsse besitzen dieselbe Avidität zu der blauen Komponente des Giemsafarbstoffes wie die Nukleolen und sind wahrscheinlich mit dem Plastin identisch. Dagegen sind die scharf umschriebenen, distinkt rot gefärbten Körnchen, die schätzungsweise eine Grösse von ¼ μ besitzen, die Träger dieses Virus selbst."

In support of their view of the parasitic nature of these minute granules they report successful transmission of the cell inclusions on some orang-utangs. In the inoculated monkeys they failed to reproduce the typical appearance of trachoma comparable to the symptoms in man. The descriptions of the microscopical examinations of the conjunctival epithelia of the infected apes are so interesting and precise that I do not hesitate to reproduce them below.

"In den nach Giemsa gefärbten Präparaten waren innerhalb der Epithelzellen neben dem Kern in dem licht blauen Protoplasma dunkelblau färbbare, nicht homogene, unregelmässige Einschlüsse sichtbar. Die zunächst kleinen runden oder ovalen Einlagerungen werden allmählich grosser, nehmen eine maulbeerförmige Gestalt an und erfahren eine mit fortschreitenden Wachstum zunehmende Auflöckerung, die im Zentrum beginnt

In der Folge sitzen sie meist kappenförmig dem Kern auf. Sodann tauchen innerhalf dieser Einschlüsse rot färbbare, distinkte, sehr feine Körnchen auf die sich rapid vermehren, die blau gefärbte Masse verdrängen und allmählich zum Verschwinden bringen. Schliesslich nehmen sie den grössten Teil des Protoplasmas ein, während die blau gefärbten Substanzen nur noch als kleine Inseln zwischen ihnen nachweisbar sind."

The above inclusions disappeared after a week and sometimes they recurred many days later.

Closely following Halberstaedter and v. Prowazek, Greeff[2] published the results of his investigations which had been carried on in Germany for many years. Greeff's descriptions of his trachoma bodies or granules are also most excellent and I wish to quote them here:

"Es handelt sich um sehr regelmässige rundliche Gebilde, die erheblich kleiner sind als die kleinste Coccen. Sie färben intensiv, bald mehr rötlich, bald mehr violett nach Giemsa, schwächer mit Anilinfarben, gar nicht nach Gram. Sie sind von einem, deutlichen, hellen Hof umgeben. Mit stärkster Vergrösserung sieht man zuweilen recht deutlich, dass sie nicht drehrund sind, sondern etwas oval, wie Bakterien mit abgerundeten Ecken. Sie verraten die Neigung, sich zu zwei aneinander zu legen, wie Doppelcoccen. In späteren Stadien liegen sie in grösseren Massen bei einander, meist intracellular in der sogenannten Hufeisenform."

Prowazek proposed to call the cell inclusion "chlamydozoa" because of the presence of amorphous masses in a sort of mantle in relation to the minute granules, the real parasites. It may appear somewhat strange that Greeff does not mention the homogeneous mass, but I have seen many instances in which the trachoma granules exist without being accompanied by this substance, and Greeff was not wrong in his descriptions just referred to, and both v. Prowazek and Greeff were dealing with the same parasitic granules. I shall come back to this point when describing our own observations.

Valuable contributions to our knowledge of the trachoma

granules have been made by further studies of Greeff, Frosch and Clausen[3], Mijaschita[4], Herford[5], Clausen[6], Greeff[7], di Santo[8], Bertarelli and Cecchetto[9], Cecchetto[10], Leber[11], Grüter[12], Leber and Hartman[13], Lindner[14], v. Prowazek and Halberstaedter[15], Heymann[16], Krüdener[17], Stanculeanu[18], Wolfrum[19], and others. Brown Pusey[20] and Verhoff[21], in America, have each reported a case of trachoma with the trachoma bodies. Except some cases of blenorrhea with and without gonococci the trachoma bodies have not been found in any other condition outside of trachoma. All investigators agree on one point, namely, the difficulty in finding the trachoma bodies in treated cases. Even in comparatively fresh and untreated cases, one may not find more than one after several hours' search through several smear preparations. In some cases they are extremely scanty, while in a few cases they may be found in every preparation.

The trachoma bodies have been found in sections by di Santo[22], Wolfrum[23], Radziejewski[24], Herzog[25], Lindner[14], and others.

Stargardt first reported a similar cell inclusion in a case of gonorrheal blenorrhea of a new born child. This finding was followed by the communications of Halberstaedter and Prowazek, and Lindner, who found the chlamydozoa in the epithelia of the conjunctiva of several cases of blenorrhea neonatorum non-gonorrhœica. Heymann also reports the chlamydozoa finding in some cases of gonorrheal conjunctivitis. Römer[26] obtained negative results in his examination of one hundred and four cases of trachoma, while Heymann was unable to find the inclusions in five out of ten untreated fresh cases of the same affection.

Our Own Observations:—With the clinical co-operation of Dr. Cohen I have been able so far to examine about three hundred cases of eye affections, including trachoma, gonorrheal conjunctivitis of new born and adults, non-gonorrheal blenorrhea, simple conjunctivitis, chronic conjunctivitis, vernal catarrh and various other forms of bacterial conjunctivitis. A large number of normal conjunctivæ of man (fifteen persons) and animals (monkeys, rabbits, cats, dogs, sheep, goats, hens,

guinea-pigs) have been examined as controls. The work in the direction of animal experiments is now in progress, and the results will be our next subject of communication.

Before presenting the results of our examinations I wish to describe briefly the technique which I found most useful for the search of the trachoma bodies.

Smears:—I employed Giemsa stain (Grübler*) twenty-four hours after which time the slides with smears are quickly decolorized in the following manner: Dip in aceton for five to ten seconds; transfer to distilled water. If overstained put in a 10 per cent. solution of glycerinethermischung (Grübler) for one or two minutes. Wash in running water for a few minutes. Blot and dry in the air. One may examine with cedar oil directly, or the smears may be mounted with cedar oil. Trachoma granules stain intensely bluish-violet, the "plastin mass" more bluish; nuclei, bright reddish-violet; protoplasm, pale bluish; mast cell granules, reddish to reddish-violet; red corpuscles, eosin color.

Sections:—Tissues are fixed in sublimate alcohol as recommended by Giemsa[27] in his recent moist method of applying his stain to smears. After twenty-four to forty-eight hours of staining the tissues pass through graduated alcohol, etc., to paraffin embedding and sectioning. Before staining the sections are treated with alcoholic iodine solution, washed in water, treated in a 0.5% solution of sodium thiosulphate, and washed in water. The sections are then stained with freshly prepared solution of Giemsa fluid (10 drops to every 10 cc. of water) with an addition of one drop of 1 per cent. potassium carbonate solution to every ten cubic centimeters of the dilution. After twenty-four hours, the slides are placed in 10 per cent. solution of glycerinethermischung (Grübler) for about five to ten minutes. The sections become distinctly reddish by this treatment. Wash the sections in water for about eight to ten minutes. Transfer the slides to aceton, aceton 70+xylol 30, aceton 50+xylol 50, aceton 30+xylol 70, and xylol, and mount in cedar oil.

*Ten drops of the stain and one drop of 1 per cent. potassium carbonate solution to every 10 c. c.

I found that by the above method the trachoma granules
may easily be differentiated from certain other granules which
otherwise may be mistaken for the former on account of minute
size and violet-staining property. This confusion which some-
times occurs in the interior of the tissue, where there may be
found scattered granules of mast cells, is eliminated by the dif-
ferentiation just described, for the trachoma granules remain
bluish-violet, while the mast cell granules become reddish-purple.
The more highly differentiated, the more bluish the former and
the more reddish the latter become. In sections the nuclei of the
epithelial cells may fail to stain in the usual reddish-violet color
as in the smears, and in this case they become rather pale-blue
after differentiation. Zenker-fixed tissues show this tendency.
In properly differentiated sections the contrast of the trachoma
bodies and other granules is most striking.

Unna's polychrome methylene blue and glycerinethermis-
chung method for mast cells also gives a satisfactory contrast
stain in which the trachoma granules as well as initial granules
are bluish, the mast cell granules are reddish, erythrocytes pale-
red, and nuclei bluish.

Other stains were not as satisfactory as the above methods.

Results.

Our findings may be tabulated as follows:

Diagnosis.		Trachoma Bodies Found.	
Trachoma—		In Smear.	In Section.
Follicular type.........180		I	I
Acute and Hypertrophic types .... 60[1]		20	16[2]
Blenorrhea—			
Gonococcal 15		0	—
Non-gonococcal 10		0	—
Vernal catarrh......... 4		0	—
Acute conjunctivitis..... 15		0	—
Chronic conjunctivitis... 15		0	—
Normal conjunctiva.... 15		0	—
	314	21	17

Remarks on the Trachoma Granules.

Smears:—The trachoma granules are principally found in the cytoplasm of epithelial cells. In a great many cells the granules group themselves in the form of a crescent or half-moon conforming with the convexity of the nucleus and almost always in direct contact with the latter. There are sometimes roundish or oval shapes as well. The size of these heaps of granules (so-called trachoma bodies), which stain rather intensely bluish-violet by Giemsa, is very variable. Some are as large as the nucleus, some very minute. On the other hand, the entire epithelial cell may be filled up with one enormously extended mass of granules. An epithelial cell may contain more than one such grouped granular mass. There are two distinct varieties of granules in a moderately large heap, one minute and one coarse. The coarse granules lie usually along the periphery, while the finer granules are within the interior. The coarse granules seem to stain more bluish, and often assume the appearance of an irregular, less intensely stainable, apparently homogeneous mass, the so-called plastin rest of Halberstaedter and Prowazek. On the other hand, the minute granules seem more uniform in size and measure, about 0.25 μ there being sometimes two together like a diplococcus. The trachoma bodies of smaller sizes are somewhat different in composition. They usually contain more of the coarse granules than of the minute sort. In some bodies the former alone are recognizable, in which the bodies appear like small rosettes stained distinctly more bluish than the advanced stage of development of the same. On the

other hand, there are some epithelial cells which are filled with
the minute type of granules. Here the number of granules may
be enormous or they may be rather sparse. The bluish staining
coarse granules at the periphery are not so numerous or often
not found. The cells appear distended and the thin wall which
is almost unrecognizable is sometimes seen to have ruptured with
the minute granules escaping around the infected epithelia. Very
frequently one sees a clear vacuolated space surrounding the tra-
choma bodies. While studying different cases I was struck with
the fact that in certain cases this vacuolization is more pronounced
than in other cases. It was also noticed that the presence of
the coarse granules and their number are more abundant in
certain cases. Thus, I sometimes found a mere heap of uniform
granules of smaller type in the cytoplasm without being associated
with bluish coarse granules. The number of such granules may
be only one or two, or they may be innumerable. This suggests
that the epithelia in this case react somewhat differently from
those in which the coarse granules predominate. In the latter
instance the invasion of the trachoma-granule is easily indicated
with the presence of the coarse granules in the infected cells.

Free trachoma granules in smears have been seen only
around the epithelia bursting with the granules, and I cannot
say that the detection of these free granules is an easy matter.

Sections:—Stained by the method I described, the trachoma
granules can be readily traced in the sections.   By the Giemsa-
plus-glycerinether mixture method, the granules are bluish-violet
in color, while other granules that may confuse the differentiation
by morphology alone will become reddish. By Unna's mast cell
stain the trachoma granules appear bluish and the mast cell
granules bright reddish. The nuclei are rather pale bluish. The
red corpuscles are pale reddish-yellow. Contrary to what
is true of smear preparations, the trachoma bodies in sections
seem always to be composed of the two varieties of granules, as
has been the case with certain smear preparations. The coarse
granules, which take the bluish stain more intensely than the
minute kind, are situated along the periphery of the trachoma

granule heap (bodies). The inner minute granules stain less bluish, but more violet with the Giemsa, and weakly bluish with the Unna method. In the early stage of development these bodies are very small, only the size of a gonococcus, and may be found scattered in a cell. In this stage the minute granules are not easily seen.

The surface layer of epithelium of the infected conjunctiva is the *usual* seat of location of the trachoma bodies. In certain regions practically every cell is infected and varying stages of development of these parasites may be found in one field. Multiple infection of an epithelial cell is very common. In a case of advanced trachoma with follicular conjunctivitis (patient Haber) I found that in the subepithelial layer where abundant small cell infiltration and active macrophagocytosis were present, there were some cells infected with the trachoma bodies of different developmental stages. These trachoma bodies were readily distinguished from any other granules by the methods I have here described. I was unable to find any trachoma bodies or free trachoma granules in the interstitial connective tissue. I have once encountered trachoma granules in a leucocyte (?) and in an endothelial cell in the follicle.

By studying a series of smears and tissues from some cases, I found that it is difficult to predict the number of trachoma bodies in tissues from the number of the bodies found in the smears. Very often I obtained a good section from a case in which smears were scanty in the bodies, and vice versa.

It is our custom to examine about four slides from each case. I often found only a single epithelial cell with trachoma bodies after a careful search of several slides. It is a most tedious undertaking, and a single microscopical examination may fail to reveal the presence of the trachoma bodies in a positive case.

PART II.—*Clinical Studies.* (*Dr. Cohen.*)

Regarding the clinical appearance of the cases studied by Dr.

Noguchi, in which the Prowazek bodies were found in smears and sections, the following classification might be considered:

I.   Follicular type.
II.   Acute type.
III.   Hypertrophic type.

I.   In the follicular type, the following condition prevails: few or numerous follicles, soft or hard (majority soft), cover a part or the entire conjunctiva—the cornea and the appendages are not involved.

There are no acute manifestations present, and the individual is unaware of any eye affection until a conjunctival examination reveals the condition.

Of this type numerous examinations were made, but the Prowazek bodies were found in only one case, that of a boy (Haber) fourteen years of age, born in this city of Austrian parents.

His conjunctiva was expressed under a general anesthetic a year ago. He received after treatment consisting of copper sulphate stick applications for two months. Treatment then ceased for ten months, when, on account of relapse or recurrence, the conjunctiva was again expressed, and the smear and section showed the Prowazek bodies.

The mother's conjunctiva was studded with numerous soft follicles in the lower lid, and a few in the upper lid, but no Prowazek bodies were found in her case.

II.   Acute type.—In this group the following symptoms were present: The lids slightly swollen; profuse serous secretion with slight pain and photophobia; intense conjunctival congestion; follicles present in the lower lid and in the retrotarsal fold; commencing infiltration in the superior part of the cornea. As a rule the Prowazek bodies were found in this group of cases.

III.   Hypertrophic type.—The symptoms of which are as follows: Lids thickened; slight serous discharge; occasionally pannus, entire conjunctiva thickened and congested; usually a few hard follicles are scattered in upper and lower lid; in this division the Prowazek bodies have been found less frequently.

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Discussion.

Dr. J. E. Weeks said that the demonstration of these tra-choma bodies was made in this country some two years ago, though not, he believed, in either New York or Philadelphia. Recently they had worked on the subject at the New York Eye and Ear Infirmary, and the bodies had been obtained, but only, he believed, in smears from fresh cases. Lindner of Vienna had demonstrated their presence in old cases as well. Familiarity

with the technique would, Dr. Weeks believed, enable us to find these bodies in a very large percentage of cases of trachoma. As Dr. Noguchi had said, they had also been found in cases of ophthalmia neonatorum which were not gonorrheal. Dr. Weeks had recently received some very beautiful drawings from Dr. Lindner of Vienna, showing the trachoma bodies in various stages, and the same bodies in the secretion of ophthalmia neonatorum. The parasite had been obtained from the conjunctiva of a monkey inoculated from the vagina of a woman whose child had the infection. While it was probable that the parasite was the cause of trachoma, Dr. Weeks did not think that it was generally accepted as such yet. Further studies must be made before this point was determined. The infectious nature of the organism, however, had been demonstrated by inoculations from trachomatous conjunctivas to the conjunctivas of the higher monkeys, as Dr. Noguchi had said. The organism had also been recovered from the eyes of monkeys which had been inoculated with trachoma from human beings.

A CASE OF HEMORRHAGIC APOPLEXY OF THE PANCREAS.

JOHN H. LARKIN, M.D.

Dr. John H. Larkin presented a specimen of hemorrhagic apoplexy of the pancreas. The patient was a man of twenty-eight years, a gambler and man about town, who presented himself at the hospital two months before, complaining of severe pain, collapse, and vomiting. He was received into the hospital, where he went into a partially comatose condition after four or five hours. The following morning the symptoms were almost all cleared up. During his four days' stay in the hospital he had attacks of collapse which were rather profound, accompanied by very low pulse and an increased amount of albumin in the

urine. There was also pain and intermittent vomiting, accompanied by some blood. He remained well from the time he left the hospital until he was taken back two days before, in the same condition. He was in extreme collapse and had a good deal of pain, especially in the epigastric region. After six or eight hours, he went into coma, and died.

At autopsy a rather peculiar condition was found when the abdomen was opened. At the pyloric end of the stomach what was at first thought to be a tumor was seen, but on further investigation it was shown that there was no tumor, but that bulging into the duodenum there was an elastic fluctuating mass which somewhat narrowed the tube. On dissecting back of the stomach the condition of hemorrhagic apoplexy of the head of the pancreas was found. The fresh clot of blood was still in position. A probe could be passed with some freedom into the upper portion of the head of the pancreas. In this area there was a fresh clot. In dissecting the large blood vessels and tracing the splenic artery, no occlusion nor lesion of the wall of the artery could be found; but on going down to the hepatic artery, and from there down, there was a marked difference of caliber, and no communication could be found from this artery into the head of the pancreas. The pancreas was very hard, elastic, and fibrous. The question arose, what had happened to this patient two months ago? At that time a large mass was felt on the left side and a tentative diagnosis of hydronephrosis was made. At the autopsy a peculiar cystic mass was found at the tail of the pancreas. Whether that mass was simply a cyst of the tail of the pancreas, or whether it was a mass which two months ago represented a hemorrhage which had become absorbed was a question.

THE EFFECTS OF SYPHILIS IN THE MENINGES.

CHARLES B. DUNLAP, M.D.

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I.

I wish, in discussing the changes which syphilis may produce in the meninges of the brain and spinal cord, to present in addition to the gummatous type, a form of meningitis of syphilitic origin which, as far as I am aware, has received little attention. It may be found briefly described among the varieties mentioned by Alzheimer in 1904, but is only casually mentioned in the literature.

Cerebral syphilis is regarded by many general pathologists as a rather rare disease. We have not found it so if we include in cerebral syphilis the effects produced by this disorder in the meninges and in the vascular apparatus. The role which syphilis plays in insane hospitals may be judged from the fact that in a material of one hundred and twelve brains received in the past year, from the State hospitals for the insane, twenty showed evidence of syphilis in the meninges, the vessels, or both; and none of these twenty cases were of the gummatous type. In this same material of one hundred and twelve brains, there were twenty-three cases of general paralysis, and twenty-seven of ordinary arteriosclerosis. This proportion of syphilitic cases (18%) is higher than would be found in the ordinary autopsy service of a State hospital. The hospitals seldom send brains from cases of manic-depressive insanity, dementia præcox, etc., to the Institute, but the cases which they do send are picked out on account of some specially interesting features. In the last one hundred autopsies at the Manhattan State Hospital (which would be fairly representative) I have not the exact number, but Dr. Rusk, the pathologist, was able to recall, without looking over the autopsy records, five of cerebral syphilis.

II.

Gummatous Form:

In the nodose or *gummatous forms* of cerebral syphilis, one may find in the meninges separate nodes of variable size presenting necrotic centers surrounded by a zone of lymphoid and plasma cells, and still more externally by more or less connective tissue; or the nodes may be of smaller size and near enough together to become confluent; or they may be of miliary size, as in a case to be shown later. With these gummatous varieties, a diffuse meningitis, or a more patchy meningitis may be associated, or (more rarely in my experience) the meninges may be essentially clear except in the close neighborhood of these nodes. The latter are situated, as a rule, in the meninges (seldom in the brain substance) and the inflammatory process is prone to invade the neighboring brain tissue both by direct extension, and by way of the vessel sheaths. In the Institute collection of over five hundred brains, we have ten examples of this gummatous type of syphilitic meningitis.

III.

The Diffuse or Non-Gummatous Form:

This diffuse type, which is more especially dealt with in this paper, consists in either a diffuse or a patchy meningeal exudate composed of lymphoid cells and a variable but usually a smaller number of plasma cells; gummatous nodes are absent. There is nothing characteristic in the cellular make-up of this exudate; it seldom contains polynuclear leucocytes, and endothelioid or phagocytic cells are relatively few. Sometimes it is most abundant on the basal surface of the brain, especially in the interpeduncular space and about the optic nerves, sometimes it is quite as abundant on the convexity. In the latter position, it will often be found in the depths of the fissures or in the neighborhood of blood vessels, especially in the loose adventitial sheaths of the latter, and in places where the exudate is massive

and the process more intense, all layers of the vessels may be penetrated by the exudate. One seldom finds a diffusely spread, abundant exudate, such as is seen in the more acute types of meningitis. Large stretches of the pia may look perfectly clear or show only fibrous thickening, and on gross examination the pia may vary little from the normal, but, on the other hand, it may be much thickened and show considerable opacity; granulations of the ependyma are usually present. There is no invasion of the brain cortex by the exudate except that occasional lymphoid cells and sometimes a few plasma cells may be found in the sheaths of these blood vessels, which enter the cortex through the meningeal exudate; these are plainly extensions of the meningeal exudate along the vessel sheaths. Often the exudate is most abundant in the pia of the brain-stem, the medulla oblongata, and the spinal cord, and in these positions it seems more prone to extend by way of the vessel sheaths into the interior.

Along with this diffuse or patchy meningeal infiltration is to be found, in the majority of cases, a girdling endarteritis of the Heubner type, the intimal tissue being firm, usually organized and laid down in concentric layers. This process in the vessels is for the most part not general, only a few vessels may show it, and those are frequently the larger branches, such as the trunks or the main branches of the Sylvian arteries, or the basilar artery. The more carefully it is looked for, the more frequently it will be found.

To summarize this form of meningitis:—it consists of either a diffuse, or, more often, a patchy interrupted exudate composed chiefly of lymphoid and plasma cells found in the meninges of the brain, brain-stem and spinal cord, and in the sheaths of the blood vessels, the walls of which it frequently penetrates: associated with it is usually an endarteritis of the Heubner type, but the arterial lesions may be confined to a relatively small number of vessels, and may be found only after prolonged search.

IV.

Differentiation:

Under this heading I shall attempt to differentiate only the diffuse or non-gummatous form, from those conditions which may resemble it.

General paralysis presents the same cellular elements in the pia, but in addition to the pial inflammation there is always a diffuse inflammatory process in the cortex and subcortex characterized by infiltration of the vascular sheaths with lymphoid and plasma cells; this general infiltration of the cortical vessels is not dependent on that of the meninges, nor is it an extension from them; it may be excessive where the meningeal infiltration is slight, in other words, there is no relation between the two; in the syphilitic forms of meningitis, on the other hand, if the cortex is invaded at all the direct relation of this invasion to the meninges is plain.

Tuberculous meningitis, especially if chronic, both in distribution and in the character of the exudate, may closely resemble the diffuse syphilitic form, but there are certain differences (aside from the presence of the tubercle bacillus) which are usually readily demonstrable in tuberculous meningitis. In the material at my disposal there is less tendency in the tuberculous process to invade the cortex and neighboring tissues, and a greater tendency to degenerative changes, the tuberculous tissue being less organized and less vascular. The cellular exudate itself contains, in tuberculous meningitis, a larger proportion of leucocytes and endothelioid cells, whereas in the syphilitic meningitis these are much in the background. Another decided difference is found in the reaction in the intima of the blood vessels, where, instead of a thick, firm resisting girdling intimal layer, such as is seen in the syphilitic cases, the endothelium in the tuberculous cases is, as a rule, merely raised and carried inwards as the result of a crowding of the subintimal tissues by cells of endothelioid and lymphoid type.

The more acute forms of meningitis would hardly come

into question in the differentiation, the character of the exudate being for the most part quite different, not to mention the presence of pathogenic bacteria, and the absence of a characteristic reaction in the blood vessels such as has been described in syphilitic meningitis. The clinical course is also entirely different. In the ordinary forms of arteriosclerosis there is no inflammatory process in the meninges.

V.

Diagnosis:

The diagnosis, on anatomical grounds, of syphilitic meningitis of non-gummatous type, consequently rests upon the presence of a diffuse or patchy cellular exudate in the meshes of the pia, and in the adventitial sheaths of the blood vessels, with, not uncommonly, penetration by the exudate into the other coats of the vessels, and the presence of an endarteritis, considered since the days of Heubner to be of specific type when found in the cerebral blood vessels. This same type of endarteritis is found in the gummatous cases; in these, moreover, there is often a diffuse or patchy meningitis of the kind described above under the diffuse form of syphilitic meningitis.

Whether or not gummata may occur in a given case of syphilitic meningitis depends upon factors which I cannot weigh; but the absence of gummata, I believe, in no way interferes with a positive diagnosis.

Concerning the clinical course of the diffuse meningeal cases I can at present say little; a fair proportion of the patients give a definite history of syphilis at a remote period; others show signs of syphilis, still others deny syphilis. In some the diagnosis of general paralysis had been made clinically, in others that of arteriosclerosis was made. This non-gummatous form of syphilitic meningitis is probably to be looked on, at least in most cases, as a late development, in the so-called tertiary period of syphilis or perhaps even beyond it.

I have not referred to the Wassermann reaction in these

cases. It has not been carried out as a rule; neither have the tissues under consideration been examined for *Spirochæta pallida*, except in a case which showed miliary gummata, where it was found by Dr. James Ewing, who was kind enough to examine some of the material. Where lumbar puncture was performed it gave a lymphocytosis as a rule. Much work remains to be done on the group both clinically and anatomically.

The lesions described were illustrated by a series of lantern slides.

A PRELIMINARY REPORT ON THE GENERAL AND SYPHILITIC FORMS OF CEREBRAL ARTERIOSCLEROSIS.

CHARLES I. LAMBERT, M.D.

(Psychiatric Institute, Ward's Island, New York.)

The aim in the study of any disease process is to ascertain in all possible detail the nature of the mechanism underlying the pathological condition. The etiology of general arteriosclerosis offers many difficulties and is only partially understood. Almost everything which is generally considered injurious and in disharmony with the constitution of the individual has been assigned as a cause. We think of heredity, of the individual's constitution, of habits and occupations, of the various intermittent or permanent physical or mental stresses and strains in life, of organic and inorganic poisons, of metabolic disorders, of intercurrent infections and intoxications, and realize that they, individually or severally, combine to favor conditions of arteriosclerosis. To trace their direct relationship, however, is well nigh impossible, largely because cause and demonstrable effect are usually remote from each other in point of time.

The fact that arteriosclerosis may occur spontaneously in the lower animals is of considerable biological interest in relation to the development of human arteriosclerosis. Lyding observed

it in cattle, horses, and dogs; while Blair, veterinarian to the Bronx Zoo, reports it as quite common in birds, especially the ostrich and emu.

Experimental medicine has endeavored to foreshorten nature's methods of producing arteriosclerosis. Numerous attempts made to reproduce arteriosclerosis in the lower animals by blood pressure stimulants and depressants such as adrenalin, barium chloride, etc., have not given uniform results which are wholly convincing and comparable to conditions as seen in human arteriosclerosis. These several reagents seem to affect primarily the media, causing degeneration and subsequent calcification of the smooth muscle fibers, together with stretching and fracture of the elastic fibers and secondary thickening of the intima. The increased blood pressure and to a less extent the toxic element have been assigned as the active factors in producing this type of arteriosclerosis.

In addition to the high blood pressure and toxic conditions, there can be little doubt that there are other factors which impair the elasticity and lower the permanent integrity of the arterial wall, notably, the infections and toxemias. The arteriosclerotic lesions thus produced are more comparable with human arteriosclerosis. Wiesel, examining the central and peripheral arteries of persons dying at the climax of acute infections, and again of other persons recovering from acute infections but dying months or years later, found in the early cases degeneration, mainly in the media, and in the later cases evidence of reparative changes.

In connection with these findings it is of importance to compare the relative effect of certain bacteria upon the different tissue components of the vessel walls. The action of certain organisms, c. g. streptococcus, pneumococcus, typhoid, etc., on the endocardium is well known; the effect upon the vessels themselves has been less studied. Some organisms seem to involve the entire vessel wall in destruction; this is more particularly true for the strictly pyogenic group of bacteria; the typhoid bacillus and pneumococcus particularly, stimulate endothelial proliferation; the tubercle bacillus, a strong connective tissue reaction,

while the *Spirochæta* (*treponema*) *pallida* may stimulate any one or all of the mesoblastic tissues to a marked activity. This tendency of certain bacteria to exert a selective action upon the different tissues is of considerable interest, not only with reference to the acute lesions but to the remote effect of such lesions in possibly increasing the vulnerability of the arterial walls in the regressive period of life.

To summarize these observations, the most evident and probable factors operating together in producing general arteriosclerosis may be classed under two main headings, first a relative increase in the strain thrown upon the blood vessel wall by heightened blood pressure, and second, an intrinsic weakness of the vessel walls due to hereditary weakness or defects acquired through disease. The action of normal or heightened blood pressure in widening the lumen of the weakened vessel locally or diffusely, depending upon the extent and distribution of the wall defects, congenital or acquired, and the reaction of the intima in a hypertrophic and hyperplastic manner to repair the defect, is the mechanism which probably underlies the development of the arteriosclerotic process. Following close upon this reparative or compensatory reaction is the essentially regressive stage which complements the vicious circle.

Under general arteriosclerosis we have what might be termed (1) a physiological arteriosclerosis, and (2) the pathological forms of general arteriosclerosis, (a) atheroma or atherosclerosis affecting the larger cerebral vessels, (b) colloid-calcareous degeneration developing most frequently in the smaller, usually medullary vessels, and (c) arteriocapillary fibrosis involving the finer arterioles and capillaries, particularly the cortical vessels.

The term physiological arteriosclerosis is used in a relative sense. The climax of growth is attained usually in the third decade of life. The completion of the normal growth is followed almost immediately by regressive changes. The parenchyma of any organ shows regressive changes relatively earlier than the conjunctival tissues, and these skeletal tissues in part at least

may be substituted for the nobler tissue elements as the latter degenerate. These changes occur earlier in some individuals than in others; in all individuals these regressive alterations inevitably lead to some degree of arteriosclerosis which may be physiological and concomitant to old age. On the other hand, vascular thickening becomes pathological when it anticipates in time, degree, and severity the physiological condition of normal senescence. Various grades of general arteriosclerosis may be seen beginning as early as the fourth decade of life, but particularly in the fifth, sixth, and seventh decades.

(a) The gross appearance of general arteriosclerosis, atheroma, as it affects the larger vessels, scarcely needs description. The lesions vary much in their distribution, sometimes affecting the larger trunks, again the medium sized and smaller vessels. If the lesions are wide-spread they are spoken of as arteriosclerosis diffusa, if scattered and localized as arteriosclerosis nodosa.

The atheromatous plaque is first apparent as a thin, gray, translucent flake on the intimal surface, later it becomes harder, of a cartilaginous appearance, and, finally, degenerating becomes yellowish and atheromatous. A transverse section through one of these plaques shows its signet-ring, non-girdling extent. Our knowledge concerning the initial changes is vague. Aside from the possible congenital intrinsic wall defects, the possibility of parenchymatous alterations and intimal reactions referable to injury is not entirely unlikely. Among the earlier changes concerning which we have demonstrable facts are those seen in the elastica and media of the vessel wall; the nuclei of the latter stain palely, and the cell cytoplasm appears cloudy, and the deeper media gradually degenerates. The vessel wall is relatively weakened at this point, dilates even under normal pressure; but in this period of life blood pressure is usually heightened. To repair and compensate for the weakened wall and widened lumen, the more responsive intima proliferates. This new-formed tissue is in no sense inflammatory; it is largely endothelial in type and origin; it has little or no plastic or stable tissue-forming proper-

ties, and uninvaded by new-formed vessels is wholly dependent upon the axial blood stream for nutrition. These conditions render the plaque peculiarly susceptible to degeneration, especially in its deeper parts. Added to these factors favoring degeneration of the endothelial plaque is the late period of life in which these changes occur. Biologically speaking, in the later period of life there is a relative weakness of the cells to regenerate themselves and especially to repair damages in a compensatory manner and resist degeneration. This is in contrast with the reaction of cells earlier in life stimulated to proliferation by a powerful irritant as occurs in the progressive, essentially syphilitic, forms of arteriosclerosis. We can, therefore, better understand why, in the later decades of life, the response to reparative changes is weaker, the product less resistant to degeneration and the end result, atheromatous degeneration, somewhat different than in the progressive forms of arteriosclerosis. The atheromatous type of arteriosclerosis affects particularly the larger cerebral vessels and is responsible for the more voluminous cerebral lesions either through softening or hemorrhage, and therefore the grosser forms of defect symptoms as hemiplegias and hemianopsia.   .

(b) In the colloid-calcareous type of general arteriosclerosis there is an infiltration of the media with a colloidcalcareous material. It appears first as fine granules in the deeper coats of the media, probably intercellularly at first, but with the accumulation of this material the granules become confluent and entirely replace the muscularis which is probably largely destroyed by pressure necrosis. With the substitution of this friable, colloid-calcareous material for the muscular coat, the resisting power of the walls is lowered and the vessel is dilated. To compensate for the widened lumen, the intima proliferates. Colloid-calcareous infiltration of the vessel wall may continue, always occurring centripetally and usually concentrically, finally resulting in obliteration of the vessel with softenings, or sometimes rupture with small hemorrhage. The lesions are naturally small, often multiple and usually isolated, and the defect symptoms correspond.

(c) In the third form of general arteriosclerosis, arterio-capillary fibrosis, the vessel walls are uniformly thickened and composed of an anuclear connective tissue, or of palely staining nuclei in a matrix of homogeneous and finely fibrillar connective tissue. It may involve a terminal arterio-capillary system and produce numerous discrete cortical and subcortical softenings. The anuclear and fibrillar character of the vessel walls, absence of inflammatory infiltrate, lymphoid and plasma cells, the type of softening, the latter usually characterized by an abundance of granule cells, the less evident tendency to a local neuroglia reaction and sclerosis distinguish it from a closely comparable condition due to syphilitic endarteritis of the terminal vessels to be described later. The lesions are discrete, patchy or diffuse. The brunt of the process falls particularly on the nervous parenchyma, and the defect symptoms, instead of being focal, may be irritative or absent; the same is likely to be true of the mental disorder of a diffuse and non-systemic character.

Under the *progressive* forms of arteriosclerosis there is the endarteritis obliterans of Heubner. The essential if not the sole cause of this form of arteriosclerosis is syphilis. Cause and effect stand in such close proximity, or if long removed from each other the specific features in their relationship usually remain so demonstrable that we may trace the life history of the process with considerable precision. The histological features of the various so-called stages of syphilis have many points in common. There is a marked reaction on the part of the mesoblastic tissues focally or diffusely manifesting itself as an infiltration of the fixed tissues with lymphoid, plasma cells and occasional mast cells, and concentric girdling proliferation of the intima of the blood vessels. The focal or diffuse character of these changes as they occur in the brain, presents anatomical and clinical varieties of syphilitic disorders. It is convenient to make three fairly distinct groups of syphilitic brain disorders. (1) The focal or gummatous type, (2) the diffuse meningeal forms, and (3) the endarteritic disorders of the larger and smaller vessels.

(1) The *focal* or *gummatous type:* The clinical complex

may closely simulate brain tumor. (2) Opposed to the focal type, is the *diffuse meningo-encephalitic* process giving rise to a meningeal complex more especially. Intermediate or combination forms of these two types are not uncommon. (3) In contradistinction to these two types, i e., the focal and diffuse, which are frankly inflammatory in nature, there are the *endarteritic* forms in which the inflammatory features are usually less evident and significant, and the tissue alterations have largely to do with the vessels themselves. The clinical features are comparable with those associated with general cerebral arteriosclerotic disorders. It is the endarteritic forms which concern us especially at this time. Two forms of endarteritis may be distinguished, (a) in which the large vessels are chiefly affected, Heubner's type, and (b) in which the small cortical vessels, Nissl's type, are involved.

A detailed study of the cerebral arteries was not made in all the cases of supposed arteriosclerosis received at the Psychiatric Institute for the past year, but in a large number of those examined, eighteen out of forty-eight cases, specific endarteritic and associated changes were found. This probably does not represent the normal ratio of occurrence at autopsy, since the material sent to the Institute consists largely of cases chosen for their clinical or anatomical importance. The histologic changes present in these cases consist of a concentric girdling proliferation of the intima of the vessels together with a more or less marked production of new elastic tissue. The amount of elastic tissue produced depends largely on the chronicity of the process. Accompanying the endarteritic changes there is usually a meso— or peri-arteritis. With this inflammatory reaction there is the development of new vessels which penetrate the new formed intimal tissue providing additional nutrition and making possible organization. The collagen fibrils of the new connective tissue thus formed are substantially resistant in themselves to degeneration and, when finally degenerating, the transformation is rather of a hyaline than a fatty nature in contrast to the fatty degeneration seen in the atheromatous process; however, the latter condition may be superimposed late in life where the individual survives the earlier endarteritic process.

The abundance of the lymphoid and plasma cell infiltrate in the vessel sheaths and pia of the endarteritic process is proportioned very considerably with the activity and age of the process, being most marked in the relatively acute conditions or those of a strikingly episodic development. It does not seem to bear any particular relation to the remoteness of the syphilitic infection but rather to the process itself. Usually, however, in cases of long standing, twelve to fifteen years, only a trace of meningitis and vascular sheath infiltration with lymphoid and plasma cells was demonstrable. This was particularly true in cases of slow development and long standing, fifteen to twenty to twenty-five or thirty-five years, lymphoid and plasma cells, especially the latter, being almost completely lacking, and mast cells in a fair number being found in addition to the endarteritic changes.

The endarteritis affecting the smaller vessels was first referred to by Nissl, but has not been described by him in detail as yet. It is possible and strongly probable that in this disorder we have a special form of syphilitic brain disease before us. It manifests itself by a tremendous endothelial reaction in the finer blood vessels of the pia and cortex especially. The original capillary wall becomes several cells thick, and new capillary sprouts are formed. The cells of the sheath grow extremely rapidly and abundantly and revert to a primitive type, thus the cells of the intima and adventitia may be indistinguishable. The nuclei are rich in chromatin, mitoses are seen, and the cytoplasm of the cell stains deeply. Rod cells are seen in the neighborhood and a relatively acute neuroglia reaction is present; comparatively few gitter and granule cells are found. Discrete or patchy softenings usually result which develop slowly and, because of the marked local neuroglia reaction, terminate rather in the form of a cortical gliosis with sclerosis than as a focal softening with the abundance of granule cells usually seen in the regressive type of arteriosclerotic softening.

The chronic aspect of this cortical blood vessel disorder is more frequently seen than the acute phase. There are several

cases in the Institute collection which very probably logically belong here. In these cases there is the history of syphilis, a characteristic endarteritis obliterans less marked in the larger vessels but conspicuously evident in the smaller cortical vessels, associated with which are numerous small softenings or areas of a diffuse cortical sclerosis which is systemic in some cases, almost general in others. The unequal involvement of the vessels, the comparatively large size of the vessel wall cells, the number of collagen fibrils in the cell cytoplasm, the absence of mitotic figures and absence of embryonic cellular features distinguishes it from the acute condition. Clinically these cases often show irritative symptoms and are usually diagnosed epilepsy, arteriosclerosis, cerebral hemorrhage, brain tumor, or stationary general paralysis. Symptoms referable to the cranial nerves and spinal cord are usually lacking, and the fewness of the cells in the pia suggests the possibility of but few being found in the spinal fluid.

Lantern slides were shown illustrating the lesions described.

THE CO-EXISTENCE OF VISCERAL SYPHILIS AND ANEURISM WITH SYPHILITIC MENINGITIS.

G. Y. RUSK, M.D.

The material which I would present is intended to emphasize the syphilitic etiology of that form of chronic meningitis of which Dr. Dunlap has spoken.

The first case presented such a meningitis with gummata of the liver and an aneurism of the arch of the aorta. The second case shows aneurismal dilatation of the basilar artery and a saccular aneurism of the middle cerebral artery at its origin.

The role that syphilis plays in the etiology of aneurism we need not discuss, but its great importance is well recognized.

The first case was that of a woman forty-nine years of age :

of late years she had used alcohol to excess and in the last three years had used morphine for control of pain in her chest, due to the aneurism. She was admitted to Manhattan State Hospital in an acute hallucinatory state, which was due to use of drugs and which cleared up within a few days of admission. She died of lobar pneumonia. The principal anatomical findings I have already indicated and I refer you to the specimen of liver and aneurism.

The nervous system was negative in the gross, except for a slight but distinct haziness of the pia over the base. Microscopic examination showed a spotty infiltration of the pia at the base, with lymphoid and plasma cells; over the convexity the inflammatory elements were scarce, but throughout there was some increased cellularity of the pia, and a slight hyperplasia of the glia of the first layer of the cortex. A study of the principal vessel trunks showed a combination of endothelial proliferation in which there is some new elastic tissue formation with the changes of the ordinary atheromatous type. Sections from the medulla and cord similarly showed chronic meningitis of the same type and of moderate grade.

The second case of aneurism of the basal vessels occurred in a man of about fifty, who after a period of depression with defective memory, lapsed into a mildly demented state. There was slight muscular weakness with spasticity on the whole right side, due to pressure of the aneurism; there was no definite history of syphilis, but the patient had suffered from headaches for a long time before admission, and his pupils were unequal and reacted sluggishly to light. On the probability of former syphilis he was given a course of anti-syphilitic medication. He died about twenty-four hours after a hemiplegic attack.

At autopsy in addition to the aneurism there was marked thickening of the pia, especially over the base and extending over the frontal and parietal lobes. There were adhesions between the frontal lobes and granulations in the fourth ventricle.

Microscopic examination of the brain tissues in this case

again showed a similar chronic meningitis of more severe grade and more diffusely distributed than in the previous case.

Study of the vessels showed in the main an advanced grade of atheroma, but one of the smaller vessels of the cortex in the frontal region showed, in addition to the atheromatous change, what appeared to be the remains of an old syphilitic endarteritis.

Lantern slides illustrating the gross brain condition in the second case and also gross preparations of the gummata in the liver and of the aortic aneurism were shown.

THE PATHOLOGY OF EXPERIMENTAL ANTERIOR POLIOMYELITIS IN THE MONKEY.

PAUL A. LEWIS, M.D.

(From the Laboratories of the Rockefeller Institute for Medical Research, New York.)

On behalf of Dr. Simon Flexner and himself, the author presented a series of lantern slides to bring out the following points developed in the course of their recent work with this subject:

I. The experimental disease in the monkey results in lesions of the central nervous system entirely comparable to those of the disease in human beings.

II. The characteristic feature of the early stages of the disease in the monkey is a perivascular infiltration with cells of the lymphocyte series. The infiltration is first seen in the pia-arachnoid and extends along this membrane and finally along the vessels into the gray matter of the spinal cord.

III. In neither the human disease nor in the monkey are the lesions strictly limited to the anterior horns. The lateral and posterior horns, the white matter, the spinal root ganglia and the pia-arachnoid are likewise involved.

A CASE OF PULMONARY, CEREBRAL, AND MENINGEAL BLASTOMYCOSIS.

G. Y. RUSK, M.D.

This case of blastomycosis occurred in a woman of sixty-three years who, after a period of general feebleness, was a patient in one of the general hospitals in the city. She is said to have become confused and talkative, and was admitted to the Manhattan State Hospital. During her two weeks' residence she was in an almost continuous comatose state with occasional episodes of low-grade delirium. The autopsy showed a brain with diffuse pial haziness, slightly more marked over the base and over the cerebellum; gelatinous masses in the lung which will be described later; acute hemorrhagic cystitis. No skin lesion was present.

In the left lung situated near the root was a group of cavities varying from the limits of visibility to 3 cm. in diameter, filled with a sticky mucoid material; for the most part they appeared inclosed in a thin connective tissue capsule, the smaller cavities were less well defined; one passed externally from the area of the larger masses into an area of diffuse thickening of the tissue, in which were scattered tiny yellow foci, suggesting plugs in small bronchi with slight bronchopneumonia.

At the time of autopsy the condition was wholly unrecognized and the process suggested a new growth, most probably a colloid carcinoma, so no cultures were taken.

Sections from the lesions found in the lungs showed the main masses of gelatinous material to be composed of a budding organism with a large capsule lying in a mucoid matrix; the walls of these cavities showed a certain amount of fibrinous overgrowth, which the organism seemed to be gradually eroding, the lining cells becoming separated and swollen, and the protoplasm finely vaculated, while the nucleus became pycnotic and gradually disappeared. One must go some little distance into the tissue before one comes upon evidence of reaction and then one finds accumulations of lymphoid and plasma cells, probably

fewer than one would expect, and a few multi-nucleated cells, but rarely is a definite giant cell seen in this region. When one passes to that part of the tissue described as diffusely firm, the microscopic picture changes considerably and one has all the elements of a chronic infective granulomatous process, including the formation of large giant cells, many of which contain parasites. Caseation is not found. Through the tissue large numbers of the organism are seen, singly and in groups. Occasional small hemorrhages are seen in the tissue. The bronchi both at the level of the first sections described and also in the second group contain parasites, and it is probable that this is the main method of dissemination in the lung tissue.

It is to be expected than an organism causing the tissue erosion, as described above, should make its way into the circulation; in the brain and meninges of this case we find the organism in great numbers.

Neither grossly nor on section, however, has any evidence of blastomycetes been found in the other organs.

In the brain the principal foci are found symmetrically situated in the basal ganglia and in the cerebellum, especially between the folia. Microscopically, however, additional foci are found in the basal ganglia, and in the cortex in a few places connecting usually with the pial invasion. The meninges particularly over the base running into the Sylvian fissures and also into the smaller fissures show a remarkable appearance. The organisms are frequently found in large masses or scattered singly; they are more or less mixed with the elements of the inflammatory exudate, lymphoid, plasma cells and large numbers of giant cells, many of which contain the organism. The meningitis is likewise marked over the cerebellum, the pons, medulla and cord again show the organism and the tissue reaction. In the lateral ventricles organisms are found with accompanying exudate.

As one passes from the base to the cortex there is a rapid diminution in the number of organisms and likewise of the reaction. Over the base where the exudate is most marked we

find no tendency to tubercle formation or caseation. About the foci in the basal ganglia a moderate reaction occurs, but it is extremely local and consists of lymphoid and plasma cells.

Of interest also is the very marked hypertrophy of the glia of the superficial layers of the cortex which occurs in response doubtless to the meningitis. On the part of the vessels no reaction of the endothelium is noticed and the perivascular infiltration seems entirely part of the meningitis.

As to the organism itself, it appears as a simple budding form, no evidence being found of sporulation or of the formation of hyphæ. The organism in this case varies from those previously found in human infection in the large capsule, which is best seen in the Zenker preserved material, while in Kaiserling or plain formalin material it is often quite indistinct; both the gross lesions and the organisms strongly suggest the form which has been found in the horse by Frothingham, who describes a large single tumor the size of a man's head, which was diagnosed as a myosarcoma and which turned out to be a blastomycotic focus from which organisms were grown.

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of the

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DR. RICHARD M. PEARCE, *President.*

LESIONS OF THE CENTRAL NERVOUS SYSTEM.*

JOHN H. LARKIN, M.D.

Dr. John H. Larkin showed lantern slides illustrating some unusual lesions of the central nervous system.

1. The first specimen was taken from a three-year-old child and showed an absence of the cerebellum on one side. On the opposite side there was absence of the olive. The pons also showed marked indentation, and there was a corresponding recession in the whole bulk.

*Presented to the Society, March 9, 1910; received for publication, April 19, 1910.

2. Specimen of the same case, higher power, showing condition of atrophy of the olive on the side opposite to that from which cerebellum was absent.

3. Section from side on which the olive was preserved.

4. Same section with higher power, showing normal contour of the pontine region on one side, but more or less loss on opposite side.

5. As is well known where there is congenital absence of the cerebellum, the atrophy goes beyond the pontine region, and there is atrophy of the brain. This specimen showed the deep part of the brain. The normal contour perfectly preserved.

6. A rather ordinary specimen of clot on the dura mater. Case of middle meningeal artery rupture not accompanied by fracture. Removed from a college student who was kicked in the head during a cane-rush. He had no serious symptoms, but was found dead in his bed the next morning.

7. Same case showing clot and dura removed, showing great compression of brain.

8. A case of rather unusual interest; an aneurysm of the basilar artery. Specimen was removed from an organist who was taken ill while on his way to church. He sat down on a stoop on Madison Avenue; he was taken to a hospital where he died. Autopsy showed an aneurysm of rather unusual size. The whole cerebellum had been rotated by pressure of the very large aneurysm. There were no pathological lesions in the brain. The cause of death was simply rupture of the aneurysm. The patient was thirty-four years old, and no history of syphilis could be obtained. This was perhaps one of the largest aneurysms Dr. Larkin had ever seen in the brain. It measured $1\frac{1}{2}$ inches in the longitudinal direction and 1 inch in the transverse.

9. Brain showing tumor posterior to both optic nerves.

10. A rather interesting brain from a boy, fifteen years of age, suffering from a spleno-myelogenous leukemia. He was taken from the street to Roosevelt Hospital in a state of coma, and died shortly after. On autopsy the case was found to be one of typical spleno-myelogenous leukemia. There was a very

large globular thrombus in the brain, dilating the ventricle to a marked degree. The thrombus could be taken right out of the lateral ventricle.

11. Case of aneurysm at base of pons with laminated thrombus taking place from one or the other of the carotid arteries. Great dilatation of the ventricles of the brain. The patient was a man, thirty-five years of age, who was found on one of the docks. This was a remarkable condition on account of the size of the aneurysm and on account of the healing process and of the absence of symptoms.

12. Another section of same brain showing laminated clot. No evidence of syphilitic inflammation.

13. A condition which is common in New York: a case of pia arachnoid hemorrhage. This is frequently met with in cases of trauma and in alcoholic individuals.

Charcot has described a condition somewhat similar and undoubtedly due to miliary aneurysms. Syphilis plays a great part in this condition. Very often the condition is not connected with trauma and is without any evidence of fracture.

14. Syphilitic leptomeningitis. The contour of the brain is normal except at the cortical part where there is depression of the brain substance. The pia arachnoid and dura are densely infiltrated. The other viscera of this individual showed multiple gummatous infiltrations in the spleen, heart, and liver.

15. Arteries from same case. There is growth of connective tissue in the intima, which has broken down.

16. Acute anterior poliomyelitis, showing absence of horn cells.

17. Higher magnification; same absence of horn cells and proliferation of glia tissue.

18. Case of chronic poliomyelitis, which had gone on for two years. In an article by Ernst a similar condition is shown, which he classes as acute anterior poliomyelitis. In reality the condition is not acute, but is chronic. One could notice complete absence of the horn cells, as compared with the opposite side.

19. After the glia tissue commences to proliferate there is complete liquifaction.

20. Section shows higher power; absolute loss of horn tissue and proliferation of glia tissue. This is a condition which may differ very greatly in different parts of the spinal cord.

21. A rare specimen of which only four cases have been described. Case of myelomalacia of the cord, somewhat approximating Landry's paralysis. The specimen was interesting because scattered all through it could be seen irregular hemorrhages. There were thrombi in the large veins, and the outline of the anterior horns in cord was entirely lost. There was thrombosis of some of the smaller veins. At different levels of the cord the condition differed very markedly. The anterior horn and bulbous condition of the posterior column could be no-of hemorrhage. At the spinal pia there was acute exudative inflammation, in some places polynuclear in type. The whole condition was one of myelomalacia due to venous thrombosis.

22. Specimen of caisson disease. Disintegration of the horn and bulbous condition of posterior column could be noticed. This also was a condition which might differ markedly at different points and levels.

23. Ordinary case of hemorrhage of brain caused by a blow on the opposite side.

24. Section from same case.

25. Case of confluent hemorrhage from blow on top of head.

26. Case of hemorrhage of brain, of three weeks' standing.

27. A somewhat common condition, known as pontine hemorrhage. Pontine hemorrhage seemed hard to explain, and on studying the anatomy it was difficult to see why such large hemorrhages should occur in the pontine region. In some cases there were very few symptoms, in other cases the symptoms were cerebellar in character. This individual had entered the hospital with symptoms which pointed to a cerebral tumor. At operation 20 c. c. of dark fluid were drawn from the cerebrum. The pa-

tient died shortly after. At autopsy no cerebral tumor could be found, but there was a great mass distending the pontine region. Dr. Larkin suggested that possibly a number of cases of pontine hemorrhage were not hemorrhages in the ordinary sense of the word as applied to other parts of the body, but depended upon a congenital condition.

28. Section of cavernous angioma of the pons of exactly the same type as that found in the liver.

PERIOSTITIS ALBUMINOSA.

JOHN A. HARTWELL, M.D.

This condition was first described in a paper by Poncet,[1] published in 1874, from a study of cases seen by Ollier. Poncet described the clinical and pathological picture of the disease, gave the name of periostitis albuminosa to it, and considered it as a specific disease having no relation to other periosteal or osteal disease. Schlange,[2] in 1887, expressed the view that the disease is similar in etiology to suppurating periostitis, and that the peculiar exudate represents a degenerative change from the pus exudate, possibly because the infecting organism is attenuated. Volkmann, Kocher, and Tavel agree essentially with this view. Vollert,[3] in an extensive study of the exudate, comes to the same conclusion. Bourlot[4] made an analysis of forty-eight cases. Of these he classed two as traumatic, three as tuberculous and forty-three as staphylococcic in origin. His view was that the disease was essentially the same as osteomyelitis, only differing from it in the nature of the exudate, and that this difference was due to the fact that the infecting organism was of a low grade of virulence. He compared the two from etiological, clinical and bacterial standpoints and demonstrated their close relation. Caillebar,[5] on the other hand, insists that all the cases are tuberculous in origin, and that the exudate is similar to the exudate occur-

ing in tuberculous irritation of serous membranes throughout the body, and often seen in cold abscesses from bone and the soft parts. These selections from the literature, which is not extensive, express the various views as to the nature of the process.

The pathological anatomy of periostitis albuminosa does not differ essentially from other forms of periostitis, except in the peculiar exudate which gives to it its name. The irritating organism may be present in the bone itself, or it may be confined to the periosteum. Some writers have believed that the outer layers of the periosteum only were affected, but the greater number believe the condition to be subperiosteal in origin. Sections of the periosteum show the same inflammatory changes as are present in suppurating periostitis. The exudate, however, differs from pus. It is often free from any cellular elements. It varies in consistency from a thin syrupy fluid to a gelatinous mass. It is transparent and straw-colored, or slightly more yellow. It contains a high percentage of proteid, often 3 per cent. and often coagulates spontaneously, this apparently depending, however, on the presence of leucocytes containing the prothrombin. The fluid is often large in quantity, and frequently forms a cyst-like cavity for itself in the soft parts. The soft tissues surrounding the bone usually show a marked inflammatory reaction to the irritation. The condition is rare, and we can find only two cases reported in the English literature, one on the dorsum of the fourth finger reported by Edington,[6] and one by Dupuis[7] occurring on the tibia following an injury. Neither gives bacteriological findings. The following three cases coming under our notice during the past two years are deemed worthy of report:

F. S., on admission to the hospital gave a history of a swelling appearing in the lower third of the left thigh about one month previously. No cause for this was known. The swelling was slightly tender and painful when walking, and there was some disability of the left knee.

Physical Examination.—Gave some indefinite evidence of pulmonary tuberculosis. The lower two-thirds of the left thigh were uniformly enlarged down to the knee joint, being three

inches larger in circumference than the right thigh at corre-
sponding points. The swelling interfered with the muscles in
such a way as to prevent full flexion of the knee. It was slightly
tender to pressure, and just above the internal condyle of the
femur the skin was slightly reddened and here was the maxi-
mum tenderness. To palpation, the swelling was hard, and gave
the sensation of a fusiform growth attached to the femur. It
was slightly more marked on the internal aspect than on the rest
of the circumference.

Operation.—Incision was made over the inner aspect of the
thigh, about three inches above the internal condyle. This was
carried down through the muscles and a large quantity of thick,
gelatinous fluid evacuated. It seemed to come from the medul-
lary canal of the femur, through two fistulous tracts. A portion
of the sac was removed for examination. It proved to be muscle
tissue showing marked histological changes, of an inflammatory
nature. The fluid planted on culture media gave a growth of
staphylococci. The wound failed to heal and two weeks later
the thigh was opened on its external aspect and in carrying the
incision down to the femur a large bone-like mass grew like a
plate from the posterior surface of the bone, and spread out into
the muscle tissue. It was separated from the soft parts by blunt
dissection, and from the shaft by chisel leaving an apparently
normal shaft intact, with the periosteum separated from the pos-
terior aspect. It was then seen that what had been taken for
fistulous tracts into the femur were, in reality, holes through this
plate of bone. Subsequently the man made a good recovery.

Pathological Report: (By Dr. Charles Norris).—The speci-
mens removed at the first operation were small and unsatisfac-
tory for diagnosis. At the second operation a considerable
amount of tissue was removed consisting of muscle tissue and
small and large bone plates and spicules. A half a test-tube full
of clear yellowish fluid was sent to the laboratory; this fluid
clotted spontaneously in the course of half an hour. The exami-
nation of the various pieces show in the main an acute inflam-
matory process, varying, however, in different places as to his-

tological detail. The muscle has undergone extensive hyaline
degeneration. Some of the muscle cells show evidences of re-
generation as indicated by multiplication of the nuclei. Many
pieces, on section, seem to be made up of an edematous and very
highly vascular tissue, the seat of extensive hemorrhagic and in-
flammatory edema. The serous exudate is in many places rich
in plasma cells, with a small number of polymorphonuclear cells.
In other places, the inflammatory process is less acute in char-
acter, showing small and well circumscribed areas of small round
cells and more or less dense masses of irregularly fragmented
nuclei.

The pieces containing bone present a beautiful example of
an active formative osteitis; the marrow spaces are lined with
rows of osteoblasts and are filled with proliferating marrow tis-
sue, showing numerous fibroblasts. This tissue without definite
bone formation is extensive and in places so cellular in character
that it gave rise to a question as to whether or not we were deal-
ing with a pure type of ossifying periostitis. The clinical and
x-ray features of the case seemed to lend support to the possi-
bility of a tumor. The final diagnosis of the condition is ossify-
ing periostitis of the femur with inflammatory lesions in the ad-
jacent muscle and tissue. The term periostitis albuminosa refers
to the character of the fluid obtained at the operation. The for-
mation of fluid of this character is an expression of irritation of
the periosteum.

We have placed under the microscope a section obtained
from a case of sarcoma of the lower end of the tibia, which was
treated with radium tubes by Dr. Abbe. The collection of fluid
was under the periosteum of the lower end of the tibia in this
case and was similar in character to that described in the case
above. The formation of this fluid in this case was possibly due
to the presence of a suppurative cellulitis resulting from the in-
sertion of the radium tubes, the fluid having collected under a
part of the periosteum not yet apparently involved by the growth.
An important point to remember in diagnosis, is that the mere

presence of such fluid does not exclude the possibility of a new growth.

W. P., male, age forty-eight. Gave a history of having noted a swelling in the upper end of the left tibia, which appeared about two years before, but it had given him no particular annoyance till he fell and struck it about three months before his admission to the hospital. Examination showed a fluctuating mass about the size of a small orange occupying the upper anterior part of the interosseus space of the leg. It showed the external evidences of being inflamed.

Operation.—An incision into the mass evacuated a thick, gelatinous, semi-transparent fluid. It seemed to be encapsulated in a cystic wall. The patient remained well for nearly a year, when the swelling recurred, and this time it grew rather rapidly to its original size. It was again incised, and a cavity containing about eight ounces of a transparent gelatinous material, varying in consistency from egg albumin to jelly, and of straw color, was found. This substance seemed to lie in a cavity bounded by the tibia, interosseous membrane, the fibula and the tibialis anticus muscle. There was no true sac. On the outer aspect of the tibia, near its head, was a roughened area denuded of periosteum, and the periosteum surrounding this was much thickened. A distinct bridge of bone grew from the tibia outward to the fibula resembling the bone plate described in the first case. The roughened surface of the tibia was curetted; the lining of the cavity was cauterized with carbolic acid, and firmly packed with gauze. A complete healing apparently took place.

The pathological examination of some of the wall of the cavity which was removed showed only chronic inflammatory changes. The bacteriological examination is not recorded. The Wassermann reaction for syphilis was positive in this patient.

D. M., age thirty-two. Suffered from typhoid fever in the fall of 1908. During his convalescence a painful swelling appeared over the outer side of the lower end of the humerus which was diagnosed as a periostitis. It never entirely subsided, but gave him comparatively little trouble for six months. Then

it grew more rapidly and became painful. At the same time a second focus appeared over the subcutaneous surface of the tibia.

Operation.—These were both opened in June, 1909. The lesion on the arm was found to be an osteomyelitis and periostitis involving the lower end of the bone. About six ounces of the same kind of fluid as was found in the other cases was present, though it was slightly more turbid. The periosteum was thickened and separated from the bone for some distance. On opening the medullary cavity the medulla was found to be slightly purulent. The swelling over the tibia was incised, and gave exit to a similar fluid, but there seemed no involvement of the bone itself.

Pathological examination of the bone and the medullary substance from the humerus showed the changes of a subacute osteomyelitis. The fluid contained pus detritus. No bacteria could be demonstrated in it, and no growth developed on culture media.

These three cases are typical of the disease. They all involved the long bones. They all showed the characteristic fluid. They were all chronic. They all involved the under surface of the periosteum. Two involved the periosteum only, while one involved the medulla also. One showed a staphylococcus, one was sterile and the third is not recorded. One occurred without previous disease, one was in a syphilitic subject, and one developed following typhoid fever. They would seem to demonstrate, so far as they go, that periostitis albuminosa is not a specific disease, but is an expression of an irritation of the periosteum by an infecting organism of a low grade of virulence which produces the characteristic albuminous exudate rather than true pus. We have no knowledge of why this is so.

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THE LESIONS OF CHRONIC ARTHRITIS.

E. H. NICHOLS, M.D.

Pathologically there are two types of changes in chronic arthritis; the first type begins as a proliferation of the connective tissue of the joint, chiefly in the synovial membrane and perichondrium, and tends to destroy the cartilage and lead to ankylosis of the joint; the second type begins primarily as a degeneration of the joint cartilage, and leads to deformity, but not to ankylosis.

There has been a great deal of confusion as to the nomenclature of the cases of chronic arthritis due, first, to the difficulty in determining the primary cause of the joint lesion. In each of the types there occurs a series of changes, and in each step of each series there may be a different clinical picture. Moreover, there has been a failure in most cases to study the pathological lesions in connection with the clinical case. Confusion also has been caused by a study of the cases solely from the point of view of the x-ray.

Although there are two types of lesions in these cases of chronic arthritis, it must be remembered that these two types do not correspond to two definite etiological factors. Many different causes may produce changes of the proliferative type, and many different causes may produce changes of the degenerative type. The only one cause producing both types, so far as my experience goes, is trauma. Moreover, one cause can produce a great variety of gross appearances and of clinical symptoms, and many causes can produce the same type of pathological changes. Another thing, the primary cause may produce partial injury to the joint, this primary injury may produce continued injury, and so the process once started may continue in a vicious circle forever.

Attention must be called to the fact that there are comparatively few structures in the knee joint. They are bone, cartilage, synovial membrane, the bone covering or perichondrium, the

membrane covering, the trabeculæ, i. e., the endosteum, and the bone marrow.

The proliferative type of joint lesion begins chiefly as a proliferation of the synovial membrane. Many causes may produce this proliferation. It may follow pyogenic infection. Infection with the gonococcus may produce lesions of this same type; the same process is seen in the so-called Still's disease; it may appear in single or in many joints in which there has been no bacterial infection; it has occurred in syphilis, and, finally, it may follow fracture. It occurs in young people and in older patients; in one joint or in many. There are undoubtedly many cases, the cause of which cannot be determined by our present methods.

There are many theories in regard to the origin of this type of arthritis. Some say that these cases are practically always of bacterial origin; some consider the cause to be faulty metabolism. In many cases it is impossible to demonstrate bacteria, though the gonococcus does cause some of these lesions. The pathological lesions point toward the probability of the theory of "faulty metabolism."

The process is as follows: a proliferation of the synovial membrane occurs, forming a layer of synovial "pannus" which grows across the surface of the joint cartilage. It may grow over both cartilages, and then these two layers may unite and lead to adhesions, or as the synovial membrane extends over the joint cartilage it may project down into the cartilage and lead to destruction, so that ultimately the bone is denuded of cartilage. Ultimately in some cases the entire joint cartilage is destroyed by this pannus.

Proliferation of connective tissue also occurs in the marrow spaces of the epiphyses, and connective tissue forms. Ultimately this proliferated connective tissue may perforate the cartilage from below, and the pannus from the epiphysis may come into contact with the pannus from the synovial membrane, so that ultimately the entire amount of cartilage may be destroyed.

Besides these two destructive processes, proliferation of the synovial membrane and of the connective tissue, there may be

proliferation of the perichondrium and of the endosteum. These two processes represent an attempt at repair and lead to new formation of cartilage and of bone. In the perichondrium the proliferation may begin in the middle of the joint so that when the joint is opened there are besides the extension of the pannus over the surface of the cartilage, raised, projected, rounded areas, due to thickening of the perichondrium, or the thickened perichondrium may at first form a rather thin, reddish looking membrane on the surface of the joint, and may later form islands of bone which may become fused with the epiphysis.

Just as there comes proliferation of the connective tissue of the marrow with the pannus, so with proliferation of the perichondrium there may be proliferation of the endosteum. This may lead at first to mere thickening of the trabeculæ, or it may accompany the new growth of connective tissue in the marrow space of the epiphysis. The changes may go on so as completely to destroy all of the original cartilage, all four layers ultimately uniting and forming complete bony ankylosis with complete destruction of the original line of joint articulation.

Hence, there are four different layers of tissue involved in this process of destruction and repair. Two of the processes represent reaction to injury, two are true reparative processes which, however, lead to destruction of the joint.

Very early in the disease there comes, as shown by x-rays, an apparent atrophy of the bone in the vicinity of the articulation. Microscopical examination of a great many of these cases shows that there is practically no resorption of the bone of the epiphysis by giant cells; on the contrary, there is in many cases a new formation of bone. The apparent atrophy is due probably only to a removal of the lime salts. The so-called atrophy of the early stages is not a true bone resorption.

As regards the capsule, there is here usually a proliferation of the connective tissue, which may vary from young granulation tissue to an excessive amount of dense fibrous tissue. The form varies according to the etiological factor. There may also be formation of the so-called synovial tags. This is, however,

very rare and much less marked than in the second type of degeneration. In the degenerative type mobility of the joint is maintained, and the joint is not destroyed. In the proliferative type ankylosis occurs early usually, and there is no chance for the development of these "joint mice."

In the other type, the so-called degenerative arthritis, the process is entirely different. It begins primarily as a degeneration and softening of the articular cartilage, with no sign of inflammation in the early stages. There may be a little inflammation later, never any of consequence. As in the proliferative type, many different causes produce these so-called degenerative cases. These changes are certainly more common in old people, in women, and in workers, than in others. This type of change may appear secondary to deposits of gout urates in the joint. It may occur in organic disease of the central nervous system, may follow trauma, or may follow fracture of the joint with great displacement of bone. The proliferative type may also follow fracture, but it is always fracture with but slight displacement. It may occur also in osteitis deformans, and in the vicinity of tumors, even without perforation of the tumor into the joint cavity.

The first change seen is a fibrillation of the articular cartilage. The constant motion of this fibrillated and softened intercellular tissue of the cartilage leads to steady erosion of the articular facets. The process may go on until the joint cartilage has been entirely softened, eroded and removed. The endosteum of the epiphysis may be thickened about the trabeculæ and so the marrow spaces may be filled up, and ultimately the ends of the bone may become thickened. As a result of these three changes, softening, destruction of cartilage, and erosion, there may occur a change in the contour of the joint, which in some cases may become extreme, but never leads to ankylosis.

Besides this fibrillation and erosion with destruction of the articular facets, there comes another change. The change takes place inside the capsule, which becomes thickened with the formation of fibrous tissue and consists in the formation of islands

of cartilage by proliferation of the perichondrium at the margin of the joint; ultimately these islands of cartilage may be converted into true bone. This true bone may be entirely denuded of cartilage.

So far as the capsule is concerned there is usually only moderate thickening, although it varies from the usual type. In Charcot's disease there is usually tremendous thickening of the capsule itself.

In these joints there is one interesting change, that is, a frequent formation of synovial tags. These tags may be formed of granulation tissue or of dense masses of cartilage or of masses of bone. Such masses may be torn off and set free in the joint cavity, as joint mice, etc. In a certain number of cases these masses are sessile and in some cases they are in the thickness of the capsule itself and not in the cavity of the joint.

So that from the cases which have been examined, it may be said that anatomically there are two types of lesions, the first beginning as a proliferation of the synovial membrane, leading to destruction and ankylosis of the joint; the other beginning primarily without inflammation as a degeneration of the joint cartilage leading to deformity of the joint without ankylosis. In either type the process tends to continue in a vicious circle.

Clinically the physician's object should be to recognize the type of lesion present; then, in specific cases, to recognize, if possible, the original etiological factor, and, when possible, to remove it.

The nomenclature used is one which seems satisfactory because it describes the pathological type of lesion. For the present the use of these two terms seemed to afford a chance for the diminution of confusion, because in all cases one would know which type of joint was being described.

Discussion.

Dr. W. R. Townsend expressed his inability to add anything to the pathological study of the subject, but he thought

that if the last word could be said as to the nomenclature of the disease from a study of its pathology, a great deal had been accomplished. The simple division into degenerative and pro-liferative arthritis was certainly very welcome. From the clini-cal standpoint the question was one with which he had had some experience. It had always seemed to him that some of the changes in the joints were related to the question of weight bearing and use, and this was well illustrated in two x-ray pho-tographs which he presented. The patient was a man of forty-two years of age who undoubtedly had a Charcot joint. This man was very active, and in the short space of four weeks, be-tween the time of taking the first and the second photographs, there occurred complete erosion and separation of the head and neck of the femur. Had the joint been kept quiet and motion prevented, one would not expect the disease to prove so rapidly destructive. The arrest of such a process, he thought, was often due to the complete rest which these patients had in the hospital ; and this was further evidenced by the way in which many of them rapidly grew worse after discharge. The question of prognosis was always interesting, and if, after further study, it could be determined with a reasonable amount of certainty what could be predicted for the future in the different types, another great step forward would be made. To be able to say, from a study of the clinical symptoms aided by x-ray pictures, that a given case would or would not improve and bony or fibrous anky-losis would or would not occur was of value.

Dr. Rufus Cole said that he very much appreciated Dr. Nichols' description of the lesions seen in cases of arthritis de-formans. He understood that Dr. Nichols felt that no close relationship could be determined between the different types of lesions and the various etiological factors concerned, though he understood that Dr. Nichols felt that the degenerative type is less frequently the result of an infection than is the other type Certain experimental work which Dr. Cole had done, he thought, had a bearing on this question, as bringing quite positive proof that the degenerative type *may* be produced by infectious agents

Several years ago, when studying the question of arthritis in rabbits, as produced by injections of streptococci, the lameness persisted in one rabbit for several months. On examining the joints of this rabbit and making an x-ray examination, a definite bony thickening with exostoses was found. The rabbit was killed and the examination of the joint showed eburnation, exostoses, and lipping of the bones, as seen in the degenerative type as described by Dr. Nichols. This case, therefore, apparently offered good proof that, under certain conditions at least, bacteria may give rise to lesions of the degenerative type.

FURTHER STUDIES OF SARCOMA OF BONE.[1]

LEO BUERGER, M.D.

What with the knowledge of the structural changes in bone that can be gained by means of the Rœntgen ray, and what with the aid of the newer viewpoints in the histopathology of sarcoma, we are in a position to-day to acquire a much more thorough and comprehensive conception of the method of growth of sarcomata of bone than has been possible in the past. In a previous publication,[2] giving observations on twenty bone sarcomata, certain characteristic features were described and their importance in diagnosis was pointed out; the utility of adhering to the histologic classification of Borst was demonstrated and a tentative grouping into seven types, each distinguished by certain definite gross morphologic criteria, was suggested as being at least of some temporary value. Since that time my own experience has been enriched by a number of additional clinical cases; two more specimens of sarcoma of the long bones have been

studied, as well as two cases of multiple myeloma. The very excellent account of Rumpel's[3] radiographic findings in bone sarcoma has been compared with the data acquired by x-ray and anatomic investigation of my own material, so that I am able to give a review based on some thirty clinical cases and forty-six specimens.

Ribbert, in his admirable inquiry into the development of these tumors, has shown that many of our old notions, particularly in regard to genesis, ought to be abandoned. Our own experiences are, in the main, in accord with his, especially in so far as they concern the probable seat of origin; but they are at variance with his conclusion in the matter of the site of inception of the so-called "peripheral" growths. We shall revert to this later on.

From a consideration of the many data before us we are led to an endorsement of a view recently advanced; namely, that true "periosteal" sarcomas are probably so rare as to be negligible, and that the bone sarcomas find their incipiency in a focus somewhere within the confines of the osseous tissue or perhaps just under the periosteal covering. Leaving aside the arguments in favor of this opinion for the present, let us assume the beginnings somewhere within the peripheral layers of the substantia corticalis, in the medulla, in the corticalis itself, or in the spongy bone, and the following structural changes will be seen to take place. There will be a disintegration and disappearance of the osseous tissue and marrow *pari passu* with the enlargement of the sarcoma, although in the case of certain varieties new bone formation either on the part of the tumor or on the part of the irritated normal bone elements may occur. The method of advance will vary in the way to be described later. Here it suffices to note that sooner or later the heterotypical cells will have destroyed some of the cortex and have found their way under the periosteum which they will lift off as they multiply. By virtue

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[3]RUMPEL: Über Geschwülste und entzündliche Erkrankungen der Knochen im Röntgenbild. Hamburg, 1908.

of this detachment (and possibly also because of the stimulation of the tumor cells themselves), proliferative changes are induced in the bone covering, and new osseous lamellæ are laid down. In the earliest stages this forms a bony thickening over the cortex indistinguishable from an inflammatory periostitic deposit. Soon, however, the neoplasm tends to encircle the bone carrying the periosteum with it. A fusiform tumefaction results, the ends of the spindle presenting on section characteristic wedges or triangular areas of periosteal bone. Later the periosteum, too, is broken, and its remnants with attached portions of new-formed bone may become included in the tumor.

In this short characterization it has been deemed advisable to call attention only to a very few but essential facts, namely: the origin in the bone tissue or marrow; the destruction of the bone and the role of the periosteum; for these will aid in the detailed study now to follow.

Turning our attention to the comparative study of our own twenty-two specimens and of the twenty-four described by Rumpel, we shall find that the tentative grouping proposed by me is also of service in classifying the tumors portrayed in that author's Atlas of Radiograms.[4] The following is the grouping under discussion.

A. Central (Endosteal) Tumors.

1. Expansive of the bone ends.
2. Expansive of the shaft.
3. Diffusely infiltrating (non-expansive).
4. Destructive, dissolutive (non-expansive).
5. Sclerosing (calcifying).
6. Perforative (non-sclerosing).

B. Peripheral.

7. Subperiosteal and true peripheral.

I. Expansive Tumors of the Ends of Long Bones.

Exquisite examples of this form are the giant-celled sarcomas usually encountered in the lower end of the femur and

[4]loc. cit.

upper end of the tibia and humerus. They begin, as a rule, in the spongiosa of the diaphysis, not far from the epiphyseal line and exhibit a marked tendency to bring about complete disintegration of the osseous tissue. By virtue of necrosis, liability to hemorrhage, and regressive metamorphosis, larger or smaller cavities are produced. As for their "expansive" nature, this needs qualification, since it is often more apparent than real. Although a moderate amount of enlargement of the extremity of the bone may be produced by the tumor or growth, even before the investing cortical sheath has been invaded, this is but meager when compared with the dilatation incident to the later destructive changes. Complete erosion of the corticalis is the result when the tumor attains considerable size. The periosteum, however, may remain as an encapsulating vestment, and hand in hand with its recession from the surface, there occurs the development of new bone, so that a new shell of thin osseous lamellæ may form the chief covering of the neoplasm. The egg-shell or ping-pong ball[5] crackle, therefore, may be elicited by pressure on either rarified cortex or new formed periosteal bone.

It is these tumors that may be easily confused with bone cysts. If we remember that cysts do not perforate, but cause rarefication and expansion of the cortex, that they are surrounded by a smooth bony wall and that reactive bone proliferation either in the bone itself or on the part of the periosteum does not occur with them, we shall have at our disposal a sufficient number of data for differential diagnosis.

That other forms of cystic sarcoma (myxo-sarcoma) and more malignant varieties (osteoblasto-sarcoma) may also belong to this group, I have already mentioned elsewhere.

2. *Expansive Tumors of the Shaft.*

A brief mention of the occurrence of expansive tumors in the diaphysis will be enough to acquaint us with this type. In

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[5]Suggested by Dr. Bloodgood.

my series there was a chondro-sarcoma of a metacarpal bone and one of the femur. In Rumpel's list there was a sarcoma developing in an enchondroma of the humerus which had much in common with my specimen of the femur. The same picture of bone destruction that is seen in the last type occurs here. The available material is hardly adequate to allow of formulating any definite rules as to what radiographic pictures ought to be expected. It is evident, however, from the data at hand, that some difficulty in the differentiation between benign enchondromas and chondro-sarcoma can hardly be avoided. In the enchondromas we not rarely encounter multiple tumors that cause disappearance of the osseous tissue leaving a structure which in the x-ray picture has a speckled and rarefied appearance. The absence of periosteal deposits is one of the most important aids in distinguishing them from many of the types of central sarcoma of bone.

Two other conditions that may simulate the central expansive sarcomas of the shaft may be mentioned: bone cysts, and cyst formation in so-called "osteitis fibrosa." The enchondromas and bone cysts both from the clinical standpoint and from the skiagrams may be practically identical, so much so that a close genetic relationship seems not unlikely. Indeed, the bone cysts are, in all probability, the end result of a number of different types of endosteal bone disease. It is not my purpose here to enter into a discussion of the differential diagnosis between these conditions and sarcoma, inasmuch as this can be best treated from a consideration of a large number of radiographic plates. Here it may suffice to call attention to the following points: that in bone cysts, fusiform or pyriform bone expansion, rarefication of the substantia compacta with the greatest absorption at the equator of the tumefaction and a distinct, a regular line of demarcation between cyst and bone tissue, are characteristic; whereas irregular expansion, perforation, extraosteal masses, periosteal bone deposits, and irregular contour are more apt to be amongst the qualities of the malignant growths.

3. *Diffuse Infiltrating* (non-expansive) *Tumors.*

Quite a contrast to the last described series is presented by those sarcomas that probably originate in the innermost layers of the substantia compacta or in the medullary substance, when they develop in the shaft, and probably begin in the *spongiosa* when they belong to the extremity of a bone. Here expansion of the corticalis is missed, and we find a displacement of osseous tissue and marrow, with marked tendency to intramedullary extension. We are often surprised, on section of the bone, to see how far in the longitudinal direction the tumor growth has advanced.

This type ought to be recognized as of clinical importance inasmuch as an early diagnosis will hardly be made. For the endosteal tumor may have already replaced a large portion of the medulla and innermost layers of corticalis, or may have caused pathological fracture long before a suspicion of neoplasm is entertained. Thus the diagnosis was made after spontaneous fracture in one case, after osteotomy in two cases, and after careful radiographic examination and exploratory incision in a fourth case. The patients do not usually consult us until after considerable bone destruction has taken place.

4. *Destructive, Dissolutive Tumors.*

When a sarcoma becomes so highly destructive that there is rapid dissolution of the whole region surrounding its point of origin, and when there is neither a tendency to expansion nor to demarcation of the neoplasm, we have a growth which may be grouped under "destructive," or "dissolutive tumors." I have seen some half dozen such sarcomas of the upper end of the fibula. The invasion of the surrounding soft parts occurs early and the tumors usually pursue a very malignant course. Rumpel's series affords two such specimens, one of the upper end of the tibia, another of the upper end of the fibula.

5. *Sclerosing, Calcifying* (ossifying) *Tumors.*

Perhaps one of the most interesting varieties of bone sar-

coma is that in which an osteoid or chondroid matrix is elabo-
rated. Hand in hand with this higher differentiation into a
typical bone and cartilage producing mesoblastic tissue goes a
tendency to sclerosis, in the sense that larger or smaller areas
of the tumor are converted into stony masses. This is accom-
plished either by a sort of lawless calcification or by the deposi-
tion of lime in the osteoid matrix and the consequent produc-
tion of a typical bone. Having already had six examples when
writing my last paper[6] (three of the femur, two of the tibia
and one of a rib), the histological and gross characteristics were
sufficiently dealt with at that time.

When these tumors make their way out under the perios-
teum they give rise to the same bone proliferation seen in the
other varieties, except that we must expect an additional osteo-
genetic process in the basal portions of tumor, namely, that
which rides on the shaft of the bone. In the extraosteal tumor
spindle the typical radiate arrangement of bony spicules is some-
times developed, especially in the chondroid varieties. That this
feature is not a distinguishing characteristic of the "periosteal"
tumors—as was formerly supposed—but belongs rather to those
central tumors that simulate the periosteal variety becomes evi-
dent to us from our analysis.

In my own collection the calcifying and ossifying type was
represented only by the osteoid and chondroid varieties, although
in one of the round and spindle celled tumors a fair amount of
irritative bone proliferation—on the part of the normal bone—
was rather striking. Rumpel pictures marked sclerosis in a
spindle celled sarcoma. Bearing in mind the fact that the sar-
comas with specialized intercellular substance, such as the chon-
droid and osteoid, may, in the course of their growth, revert to
immature, low types (spindle and round celled forms), and that
we not infrequently find soft immature sarcoma in the metas-
tases and extraosteal masses, it seems possible that osteoid or
chondroid substance may be overlooked if the central portions

[6]loc. cit.

—or the oldest parts—are not subjected to histological examination.

VI. *Perforative Endosteal Tumors.*

Instead of a large central focus causing expansion, or diffuse endosteal infiltration, or extensive bone destruction, or sclerosis, we may see a totally different picture : namely, a small intraosteal mass causing early perforation. In the analysis of Rumpel's sarcomas it was found that this type is not at all unusual. Seven of his tumors could be placed into this class, two of the tibia, two of the humerus, and three of the femur. In all of them the sarcoma had its origin in the spongiosa of the diaphysis and there was a relatively small endosteal focus with large extraosteal masses. The other features already sufficiently described can be readily detected by a glance at the illustrations.

We need hardly emphasize the difficulty and, in most cases, the impossibility of diagnosticating this type of sarcoma before perforation has taken place. When the humerus is affected, the recognition of the condition, even with radiograms, may tax our powers to a still greater degree. The meager changes in the bone may go with considerable tumefaction of the soft parts and the diagnosis of arthritis may be made.

VII. *Peripheral Tumors.*

Having had but one tumor whose origin was either "subperiosteal" or in the outermost lamellæ of the cortex, it would have been audacious to have expressed myself decisively in regard to the moot point of periosteal or peripheral origin in my first paper.[7] Comparing my own specimen with those described by Rumpel, the conclusion is inevitable that a certain percentage of the bone sarcomas do belong to this class, and that in a series of eight tumors, at least, the periosteum, although affected by the growth, is not the seat of its inception.

Is it always possible to distinguish the lesions of sarcomas of small extent from those that belong to a traumatic or inflam-

[7]loc. cit.

matory periostitis, in skiagrams? The differential diagnosis may
be difficult, for the shadow pictures may show only periosteal
deposits without appreciable changes in the bone itself. The cir-
cumferential type of bone deposit usually speaks in favor of
neoplasm, whereas in the traumatic periostitis we are more apt
to find irregular, and possibly multiple, patches of bone deposit.
However, it is clear that, even in sarcoma, the very earliest peri-
osteal lesion will not have encircled the shaft, and the beginnings
of the neoplastic lesion may, therefore, be difficult of diagnosis.

General Considerations.

Having thus outlined the characteristics of forty-six bone
sarcomas, and having grouped them according to gross morpho-
logical traits, it may be well to gain a broader impression of the
subject by tabulating both our own specimens and those of Rum-
pel and by giving the subject of classification and point of ori-
gin more critical consideration. The distribution was as follows:

	Rumpel.[8]	Author.[9]	Total.
Femur	8	11	19
Tibia	5	4	9
Humerus	6	1	7
Fibula	2	4	6
Metacarpal	1	1	2
Radius	1	0	1
Ulna	1	0	1
Rib	0	1	1
Total	24	22	46

In order of frequency we would have femur, tibia, humerus,
fibula, and metacarpal. Reinhardt[10] collected fifty-four cases in
which there were nineteen of the tibia, eighteen of the femur,
thirteen of the humerus, and two each of the fibula and radius.

[8]Includes only those critically studied by me, the data being sufficient.

[9]The multiple myelomata are not added. Only specimens which were
studied anatomically were included in my list.

[10]Deutsche Zeitsch f. Chir., 1897, Vol. 47. p. 523.

Muller,[11] in reviewing two hundred and nine sarcomas, found the tibia affected seventy-seven times, femur seventy, humerus thirty-eight, radius eleven, ulna six, and fibula eight. The tibia and femur, therefore, take the first place, followed by the humerus, and then by the fibula and radius.

Has the comparative study of this larger number of bone sarcomas given impressions that would tend to strengthen notions already obtained through our previous investigation? We must answer in the affirmative. A suspicion has arisen that perhaps certain of the groups do not possess any essential properties with which the gross alterations are inseparably linked, and that the changes of bone architecture depend for the most part on variations in the site of origin of the neoplasm. However this may be, the establishment of the existence of important widely variant forms is not nullified; and we must concede, that, although the assumption as to the effect of origin may be true in the case of the "border-line" tumors, most of the neoplasms possess a sufficient number of distinctive qualities to allow of the grouping adopted by us. Tabulating Rumpel's tumors and my own, we find the forty-six sarcomas grouped as follows:

I. *Expansive of the Extremities of Bones.*

	Rumpel.	Author.
Femur	2	3
Humerus	1	..

II. *Expansive of the Shaft.*

Humerus	2	..
Femur	..	1
Metacarpal	..	1

III. *Diffuse Infiltrating.*

Femur	..	2
Tibia	..	1
Humerus	..	1
Ulna	1	..

[11]Muller, Wilhelm.

IV. *Dissolutive* (destructive).

Fibula	1	3
Femur	..	1
Tibia	1	1

V. *Sclerosing, Ossifying, Calcifying.*

Femur	1	3
Tibia	1	2
Rib	..	1

VI. *Perforative Endosteal.*

Femur	3	1
Humerus	2	..
Tibia	2	..

VII. *Peripheral.*

A. Subperiosteal[12] (shaft)	1	1
B. True peripheral:		
Femur (shaft)	1	..
Humerus (shaft)	1	..
Radius (shaft)	1	..
Tibia (shaft)	1	..
Fibula (shaft)	1	..
Metacarpal (shaft)	1	..
Total	24	22

Rather striking is the large number of perforative endosteal tumors of which I have had but one example, and of which Rumpel—if my interpretation of his radiographic findings is correct—has had seven. This augmentation in the number of examples of a type which had to be separated from the rest in my series (although there was only one) makes it certain that this variety is to be reckoned with. None the less remarkable—and a circumstance which has somewhat altered my former concept —is the large proportion of peripheral sarcomata, seven out of twenty-four, as compared with one out of twenty-two in my list.

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[12]With very slight or practically no erosion of the substantia corticalis.

In the bony tissue the sarcoma elements soon cause a disappearance of the normal structure, with a rapid resorptive process, the bone melting away, as it were, before the advancing cells of the neoplasm. The bone absorption seems, for the most part, to be the result of the direct action of the tumor cells, although we not infrequently see osteoclasts engaged in a similar process. At the same time an interesting phenomenon may occur, namely, the deposition of new matrix upon the very bone tissue that is undergoing destruction. Such osteoplasia needs careful interpretation since it may either be a normal reactive homeotypical bone proliferation, such as is the rule in syphilis and chronic inflammatory processes, or may be heterotypical or atypical, the result of the activities of bone forming, osteoblastic sarcoma elements. The former type is usually not sufficient in amount to produce architectural changes that need special consideration from the standpoint of diagnosis in the skiagrams; the latter, on the other hand (belonging par excellence to the osteoid, chondroid and true osteosarcomata), is responsible for the striking lime and bone metamorphosis which has already received special mention elsewhere.

By virtue of advance through Haversian canals or by direct extension through places in the *substantia corticalis* that have undergone complete absorption, the neoplasm finds its way under the periosteum. The latter becomes separated from its bony support, first over a small area, and then either by reason of the progress of the tumor, or because of hemorrhages between it and the surface of the bone. It is now that the peculiar phenomenon of new bone formation under and by the periosteum takes place. A study of the skiagrams of gross specimens reveals the interesting fact that the bone deposition occurs in two forms; either as flat stratified lamellæ, disposed parallel with the long axis and surrounding the bone, or, in the shape of fine trabeculæ that have a radiate arrangement, lying perpendicular to the shaft. Both of these varieties can frequently be found in the same specimen. Although my studies of this particular phenomenon cannot be regarded as sufficiently thorough

to warrant a decided opinion, it seems to me now that the fol-
lowing explanaton will hold good. The flat lamellæ represent,
in part, bony deposits that are the result of bone proliferation
from the peripheral layers of corticalis, and, in part, the pro-
liferation that occurs when the periosteum has suffered but mi-
nute separation from the bone. Such separation is not confined
to the immediate variety of the perforating sarcoma tissue, but
extends for a considerable distance up and down the shaft and
in a circumferential direction. Thus the first consequence of
cortical perforation will be the growth of a thin plate of bone
upon the shaft. As the tumor enlarges, a tendency to form a
lenticular shaped growth becomes manifest. The periosteal ele-
vation may occur at intervals, depending upon the subperiosteal
tension, and each fresh act of separation will be followed by a
new accession of lamellar bone growth. Simultaneous with this
another modus of periosteal activity is evidenced in the growth
of bone trabecula from the periphery toward and perpendicular
to the bone. Such radiate disposition is particularly shown in
the radiograms and, according to Ribbert, depends on the fact
that the perforating vessels have been pulled out in that direc-
tion and must, to a certain extent, determine the direction of
growth. Be that as it may, we need but note that where the
bone covering has suffered any considerable displacement, there
the radiate arrangement is purely missed, whereas where the
periosteum is separated but a few millimeters or less than a mil-
limeter, the lamellar structure is more apparent.

At the poles of the extraosteal tumor, where the transition
between normal and uplifted periosteum must be sought, there
a characteristic wedge (in section) or conical shell of bone is
regularly seen. The importance of recognizing this structural
marking both in diagnosis and in the estimation of the site of
origin will receive attention later on.

We have thus far called especial attention to the prolifera-
tive phenomena induced by the extraosteal growth. It can read-
ily be appreciated, however, that the new formed periosteal bone
will in its turn suffer the same destruction which had already

befallen the existing osseous tissue. As a result, the central
parts of the cortex of extraosteal spindle will become deprived
of its bony covering, a fibrous capsule, the last remnant of peri-
osteum may be left or rupture of this may occur, in consequence
of which a rapid growth into the soft parts, or around the peri-
osteum occurs. The periosteum then lies in the tumor mass.
This explains the occasional inclusion of periosteum with its ad-
herent bone in parts of extraosteal tumors.

From this description it is evident that, if it is possible to
determine the presence of intact periosteum, or to detect evi-
dence of bone proliferation in it, or to trace its dislodgement in
the manner suggested, we must be prepared to controvert the
opinion that such periosteum contains in it the nucleus of incep-
tion of the neoplasm. We must rather seek a focus under the
periosteum or in the bone itself.

Of the extraosteal tumors the fusiform type is the ordinary
variety. This form may give us—as will be seen later—no in-
dication as to where the beginnings of the tumor lie. Whereas
the true spindle, with tapering ends, may be found when the
tumor is limited to the shaft, a blunt, and even fungiform over-
hang may mark its limit at the extremity of a long bone. The
absence of the typical periosteal bone wedge may be ascribed to
the dense adhesion of the membrane at the epiphyseal region.
Besides this we need only mention the nodular, lobules of extra-
osteal metastases, occasionally seen, and the irregular forms that
belong to the stage of periosteal destruction and infiltration of
the soft parts.

The Origin of the Bone Sarcomata.

In the light of what has been said we can now better under-
stand the presumptive point of origin of the tumors belonging
to our series. Fortified with the knowledge of the rôle played
by the periosteum in the development of the bone sarcomata,
we must abandon the old conception of division into myeloge-
nous and periosteal varieties. Ribbert recognizes central and
peripheral forms. The former originate in most instances in

the substantia spongiosa of the diaphysis, although they may grow from any point that lies within the outermost layers of the periosteal bone. Ribbert would have even these so-called peripheral tumors start near one end of the diaphysis and creep up or down the shaft. I shall be able to show that at least this latter view is not in accordance with the data at our disposal.

In establishing the location of the beginnings of the malignant tumors, we must bear in mind a few fundamental facts. A tumor will grow with equal rapidity in all directions, if the resistance offered on all sides is approximately the same. It is just here in the sarcomas of bone that we encounter several difficulties in the proper interpretation of the point at issue. These are the differences of rate of proliferation in bone, and in soft parts, and the limiting powers of the substantia compacta, of the articular cartilage and the periosteum. Thus we cannot offhand place the site of initial growth in the center of the gross product.

Turning to our series, the expansive tumors of the ends of the long bones will be found to arise from a point somewhere in spongy bone of the end of the diaphysis. Beginning, for the most part, in the upper end of the tibia or lower end of the femur, the equal enlargement will leave no doubt as to the correctness of the assumption that they are central in origin.

When we come to consider the expansive tumors of the shaft and the diffuse infiltrating type, we meet with a more intricate problem. Here we may assume a focus either in the marrow, in the innermost layers of the *substantia compacta* or in the spongiosa of the diaphysis. In view of the nature of the histologic types (giant-celled and chondral), it seems most likely that an osseous rather than myelogenous focus is their starting point.

The dissolutive form also arises in all probability in the spongiosa of the diaphysis. The equal destruction of the bone ends is sufficient testimony in favor of this view.

Perhaps none of the tumors afford as much food for investigation as the sclerosing and ossifying sarcomas, when they

form fusiform bone encasing spindles, or when they cause that fusion of calcified tumor and bone that makes the identification of a neoplasm so difficult. Here we meet with growths that show both endosteal and extraosteal proliferation. The focus in the bone may be smaller than the mass without. In the interior of the bone there is usually calcification, and often greater in extent than that which forms the petrified core of the extraosteal masses. In these forms the dense nature of the intraosteal fo-cus and the evidences of cortical perforation and the separation of the periosteum leave little doubt that they are endosteal in origin.

Exquisite examples of endosteal origin are given us in the perforative type, in which the central focus is usually much smaller than the extraosteal mass. Here we are not aided in our estimation of the age of the new growth by such a phe-nomenon as calcification. When we study the relative size of extra- and intraosteal neoplasm and keep in mind the greater rapidity of growth outside of the bone, we shall be forced to find the point of origin within rather than outside of the bone.

Thirty-eight of the forty-six tumors under consideration, therefore, have their inception at points lying either in the spongy bone, in deepest layers of the compacta or possibly in the mar-row. My own series (as was already noted in a previous pa-per)[13] shows but one example of a neoplasm which is not central in origin. At that time our experience did not warrant any de-cisive conclusions either as to the question of the recognition of periosteal growths or as to the frequency of those that might be classed either as subperiosteal or peripheral. The additional facts gained in the analysis of Rumpel's specimens permit us to take the view that sarcomas do arise from the peripheral layers of the substantia compacta, usually in the shaft; and that Ribbert's assumption of a site of origin in the extremity of the long bones is untenable, at least as far as our own material is concerned. We encounter two types in the eight neoplasms be-

[13]loc. cit.

fore us. In the first there is a subperiosteal tumor without apparent destruction of bone, and in the second the tumor is associated with those osseous changes that are indicative of the neoplasm's destructive growth.

When we find a broad sessile, or fusiform tumor on the shaft, with the signs of periosteal detachment, bone proliferation and cortical erosion, we are led to refer the starting point to the outermost layers of the compacta. In none of the specimens analyzed can we place the point of origin near the extremity of the long bone, and we are forced to the conclusion that the outermost layers of the corticalis should be regarded as the point of origin of the so-called peripheral forms.

Let us review briefly the grouping into seven classes and inquire as to whether these will now stand the test of more careful investigation. Are the points of distinction that permit of this subdivision essential characteristics, are they purely fortuitous, do they depend wholly on the histological variations, or are they in great part but the expressions of differences in situation of the very beginnings of the growths? From what has already been said it is clear that the architecture of the sarcoma and the bone, as we see them, will not be fashioned by any one of these factors, but will show the effects of a combination of several or all. The utility of any grouping, it appears to me, must be estimated especially from the standpoint of value in diagnosis, and of value as an aid in remembering the types. A histological classification is practically useless in this regard.

The expansive types are sufficiently characterized by the absence of tendency to early perforation. The diffusely infiltrating growths may be said to remain confined to the interior of the bone because they arise in the deeper layers of the cortex, in the marrow, or in the middle of the spongiosa. That the site of origin must determine this peculiarity of remaining endosteal to a great extent cannot be denied. However, the late perforation, the slow invasion of the compacta, the extensive intramedullary involvement, the striking difference between the development here and in the dissolutive and perforative types, these facts war-

rant making a separate class of these forms. The fourth group
—the dissolutive type—presents a marked contrast to the ex-
pansive type and merits, therefore, the special consideration
which it has received. It might be urged that, were this type
to owe its inception to a focus near the cortex, the perforative
endosteal variety might result. We must grant this to be the
case, and that this criticism is not a negligible one. We need
hardly pause to discuss the utility of recognizing the sclerosing
type; for the diagnostic points brought out by a study of the
pathology of these tumors have been dwelt upon elsewhere. As
regards the perforative endosteal tumors, can the gross struc-
tural changes be explained altogether by the assumption that
here, too, the initial process is nearer the periphery than the
center of the bone? It seems that a difference in site of origin
cannot be the only factor. For is it not striking that in the
case of certain varieties (the diffusely infiltrating—and expan-
sive), a marked resistance is offered by the cortical shell, where-
as just here early penetration occurs? It would be possible to ex-
plain the configuration of these tumors only by supposing a be-
ginning in the cortex itself. The relative size of extra and in-
traosteal masses will not permit of such an hypothesis in all
cases. In those instances in which an extraosteal tumor is not
very much larger than the endosteal mass the growth could hardly
start so near the periphery, for the progress without must be
much more rapid than within the bone. All in all, it seems best
at this juncture to call attention to this variety by means of spe-
cial grouping, leaving the final adjudication of the admissibilty
of such grouping until more specimens shall have come under
observation.

Finally, a word as to the peripheral forms. Ribbert in-
cludes here all those sarcomas that originate in bone of perios-
teal origin. Inasmuch as it becomes practically impossible to de-
cide the exact point of origin from the study of the specimens,
and a certain latitude of error must be allowed, such a basis for
distinguishing the peripheral varieties seems inadequate. From
a consideration of my own material and the study of the avail-

able data given by Rumpel, it would be best to include in the peripheral class only those neoplasms which show either sub-periosteal growth without change in the bone, or subperiosteal growth with those typical erosive lesions that indicate to us a genesis in the most superficial layers of the cortex.

Discussion.

DR. JAMES EWING, after expressing his admiration for Dr. Buerger's careful work, asked him whether it was not possible that some of the seven varieties which he had described might be representative of different stages of the same process, and further whether a close study of the histology of the tumors might not furnish evidence which would enable him to group together and perhaps reduce the number of the classes.

DR. CHARLES NORRIS asked how Dr. Buerger was able to determine the older portions of the growth, of which he had spoken several times.

DR. BUERGER said, in regard to Dr. Ewing's query as to whether some of these classes might not represent various stages of the same process, that he must admit that he had himself made the same criticism. Time had prevented him from going into this matter minutely. Briefly, however, it might be said that expansive tumors were, of course, sufficiently characteristic; they certainly differed materially from the rest. The same could be said of the sclerosing type. The only trouble would arise in differentiating the diffusely infiltrating variety, the destructive variety, and the perforative type. As regards the perforative endosteal tumors, can the gross structural changes be explained altogether by the assumption that here, too, the initial process is nearer the periphery than the center of the bone? It seems that a difference in site of origin can not be the only factor. For is it not striking that, in the case of certain varieties (the diffusely infiltrating and expansive), a marked resistance is offered by the cortical shell, whereas just here early penetration occurs? It would be possible to explain the configuration of these tumors only by assuming a beginning in the cortex itself. The relative

size of extra- and intraosteal masses will not permit of such an hypothesis in all cases. As to the other two: the destructive forms are characterized by early destruction of the cortex, which is in marked contrast to the infiltrating forms. This peculiarity and their intense dissolutive powers permit of placing them in a class by themselves. As to whether something more could not be learned from a study of the histology of these tumors, in the way of correlating histological and gross types, Dr. Buerger said that he had not had much success except in the osteoid and chondroid forms where there is the intense calcification and bone formation. The other forms could not be associated with histological changes. In regard to the possibility of distinguishing the older portions of the tumors, Dr. Buerger said that this could be done only in the osteoid tumors where the oldest portions were accompanied by the greatest amount of calcification, whereas the younger parts were soft.

FILARIA IN SECTIONS OF INGUINAL LYMPH NODE.

B. C. CROWELL, M.D.

The case for presentation refers to a native of the Danish West Indies, thirty-two years of age, who was admitted to the hospital service of Dr. Hayden for a swelling in the right groin, which he had had since a boy. He has been in this country six years. This swelling has been treated by cupping a few times with temporary improvement, and at one time, it was opened and a small amount of blood expressed. He had large femoral and inguinal nodes on the right side, over which there was considerable edema. His right epididymis was enlarged, hardened, and nodular. There was some thickening of the right spermatic cord and evidence of moderate left-sided hydrocele. A few of the very large inguinal nodes were removed for diagnosis. On routine section of these, which showed a chronic hypeprlastic

lymphadenitis, there was discovered in a very much thickened
and dilated lymphatic a section of what is apparently a nema-
tode worm which corresponds to the descriptions of *Filaria Ban-
crofti* coiled on itself.   It consists of a musculo-cutaneous mar-
gin enclosing a thin-walled bilobed uterus and an alimentary
canal whose walls are pigmented.   The uterus contains numer-
ous ova and embryo filariæ, some of which can be seen outside
of the parent worm in the lymphatic space.   The lymphatics
show very well the characteristic connective tissue and muscular
thickening.   Further examination of the patient was not made,
aside from a single afternoon blood examination which showed
no leucocytosis and 8.5 per cent. of eosinophiles.

Very few cases of such findings have been recorded.   In
1900 Lothrop and Pratt reported finding of worms in the epi-
didymis; and in 1901 Opie also found worms in the epididymis
associated with an immense lymphatic varix involving the tho-
racic duct and all of the retroperitoneal lymphatics and extend-
ing into the scrotum.   One other case of accidental finding of
the parent worm in the hardened tissues was previously reported.
Dr. James Ewing said that he had had a similar case at the
Cornell Medical College six years ago.

EXTENSIVE THROMBOSIS OF THE CERVICAL
VEINS FOLLOWING (a) ACUTE AND (b)
CHRONIC OTITIS MEDIA.

B. C. CROWELL, M.D., AND A. B. EISENBREY, M.D.

(a) We are enabled to report the following case through
the courtesy of Dr. H. M. Taylor.

B. L. I., male, aged twelve years, during convalescence from
an attack of measles of average severity, developed a high ir-
regular temperature with symptoms referable to a right-sided
otitis media with mastoid infection.   When the condition had
continued for five days, operation was decided upon.   It was

found that the external jugular vein on the right side was thrombosed and that abscesses were present in the right hand and right ankle. In addition to the mastoidectomy and opening of the right lateral sinus, phlebectomy was performed and the abscesses were drained. After operation there was temporary remission of the acute symptoms, followed by recurrence and death on the fourth day.

Autopsy.—Cause of death: Septicæmia (streptococcus); otitis media, acute suppurative, right side; thrombosis of lateral and petrosal sinuses, right side; thrombosis of cervical veins; pericarditis, fibrino-purulent; endocarditis, acute mural and valvular; acute parenchymatous degeneration and abscess of heart muscle; bronchopneumonia, terminal; acute splenic tumor; acute parenchymatous degeneration of liver; acute parenchymatous degeneration of kidneys; abscess of right hand, right ankle, and left gluteal region.

Smears from pus of middle ear showed numerous streptococci and a few staphylococci. Smears from lung showed a few streptococci, numerous pneumococci and large numbers of staphylococci. Culture of blood from heart showed a pure growth of streptococci.

The brain, with the exception of a small area of softening directly beneath the operative field, where the anterior margin of the right side of the cerebellum lay in contact with the lateral sinus, showed no macroscopic lesions further than a general congestion of the pial vessels. The cerebrospinal fluid was clear. No thrombosis of the cerebral vessels or abscess formation was found.

The longitudinal sinus contained considerable fluid blood and a small chicken fat clot. On the left side of the cranial cavity all of the sinuses were free and contained fluid blood. On the right side the lateral sinus contained a firm thrombus extending from the point where it had been opened into backward to the torcula, and anteriorly both petrosal sinuses were thrombosed. The middle ear on the right side was the seat of an acute suppurative process which had extended backward into

the cancellous bone. On the left side the middle ear appeared normal.

The heart contained fluid blood and in the right ventricle a small chicken fat clot was present. No thrombosis of the pulmonary vessels or infarction of the lungs was found. After removal of the heart, the superior vena cava was examined and found to contain a firm mass which, when grasped by forceps, was readily removed and revealed a thrombotic cast of the cervical veins. Unfortunately the early removal of the mass made it impossible to ascertain just which of the cervical veins were involved in the process, and dissection of the neck which might have revealed further evidences of thrombosis of the vessels was not undertaken.

The specimen presented consists of the cast of the cervical veins made up of the thrombus which was removed as previously described. Its appearance indicates that the process was more extensive and that, in removal, parts of it were broken off and remained in other branches of the vessels.

(b) The case for presentation is that of an Irish woman, forty-five years of age, who about four years ago was said to have had an attack of meningitis, since which she had had marked loss of memory and had complained of her right ear, saying that it "felt as though stuffed up." At no time was deafness or a discharge noticed. She also had extensive ulcerations on the leg, which had been skin grafted. Her admission to the hospital was on account of her leg condition and while in the hospital she was regarded as a case of endocarditis, on account of the irregularity of the heart and the presence of a systolic murmur over the precordium.

At autopsy she was found to have an extensive thrombosis, involving the entire superior vena cava, both innominate, external and internal jugular veins, the right lateral sinus, and the temporo-sphenoidal and occipital veins. She had a chronic right-sided otitis media and mastoiditis; there was no cerebral or meningeal congestion or edema. The other lesions present were slight parenchymatous and chronic interstitial nephritis; double

hydrothorax and nutmeg liver. The thrombi were old, definitely adherent, mixed thrombi, firmer and paler in the portions near the heart than in the cranial vessels.

Cultures made from the spleen and innominate veins show small curved and clubbed Gram positive rods, resembling pseudo-diphtheria bacilli, but the relation of these organisms to the thrombosis was not determinable. Microscopical section of the innominate vein with thrombus shows an extensive chronic phlebitis, with loss of the endothelium at the point where the thrombus was attached, breaking up of the internal elastic layer and a considerable disintegration of the media with thickening and thrombosis in the adventitia.

A CASE OF CHRONIC OR UNRESOLVED PNEUMO-NIA, POLYSEROSITIS, AND SENILE MAL-NUTRITION.

JAMES EWING, M.D.

The term unresolved pneumonia is not always applied to the same condition. By some it is used to designate a type of pneumonia in which the exudate consists chiefly of a homo-genous fibrinoid material very poor in leucocytes, which is fol-lowed by organization of the exudate by spindle cells, prolifera-tion in the walls of air vesicles, fusion of plugs of exudate, and gradual contraction of the involved pulmonary lobe into scar tissue. More often the patient dies in the acute stage of this pneumonia, and cicatrization never occurs. Several years ago Delafield showed that this type of pneumonia is a specific variety and is not merely a failure of resolution of an ordinary lobar pneumonia. Slightly delayed resolution of an ordinary pneu-monic exudate is probably not an uncommon event, but persist-ent failure of resolution in a lobar pneumonia extending over

many weeks, and even many months, is extremely rare, so that the present case illustrating persistence of an ordinary lobar pneumonia for about fourteen months seems to be worth recording.

The patient was a man, sixty-one years of age, who had suffered for several years from indigestion and malnutrition which reached such a grade that he eventually became extremely emaciated. No definite cause of this trouble could be discovered by various specialists here and abroad. During 1908 the vision in the right eye became impaired, and in July, 1908, this eye was removed for a condition which some regarded as syphilis. The ocular lesions consisted in a productive round cell inflammation of much of the choroid with detachment of the retina.

In November, 1908, he was taken acutely ill with fever and signs of consolidation of the right lung. These signs and symptoms continued irregularly until his death in January, 1910. During this period of about fourteen months he was seldom free from fever and dyspnea, and was confined to bed. For many weeks he received pneumococcus vaccines. After the subsidence of the acute symptoms the attention of his physician was drawn away from the pulmonary condition to his progressive emaciation which reached an extreme degree, the body finally consisting chiefly of skin, bones, and extremely thin ribbon-like muscles. There were arthritic symptoms, pains, loss of reflexes, and ataxia, which suggested tabes. The Wassermann test was negative. The urine was free from albumin and gave no indication of renal disease. The heart's action was accelerated and weak. There were constant moderate dyspnea and numerous attacks of severe dyspnea which the patient could be induced to overcome by voluntary efforts at respiration. There was no hypertension. The feeding of the patient was accomplished with great difficulty, as he would eat little of anything. Ingestion of meat or eggs was sometimes followed by severe indigestion and intoxication, so that this form of diet had eventually to be omitted altogether and he was given small quantities of fruit and cereals. During the last three months there was little fever. During the

last month there were several syncopal attacks with dyspnea in one of which he finally died.

The anatomical diagnosis at autopsy was as follows:

Partial pneumonic consolidation of right lower and posterior portions of upper lobe. Extensive chronic fibrinous pleurisy over both lungs, especially the right, with slight serous exudate over right. Universal adhesive pericarditis. Chronic mediastinitis. Chronic perihepatitis binding upper surface of liver to diaphragm. Chronic perisplenitis causing constriction of colon. Dilatation of stomach with atrophy of gastric mucosa. Advanced chronic diffuse nephritis of right kidney. Nearly complete atrophy of left kidney. Extensive hyperplasia of adrenals. Marked atrophy of pancreas with preservation of islands of Langerhans. Marked sclerosis and atrophy of thyroid.

Microscopical Examination.

The consolidated portions of the lung show an exudate filling the air vesicles, composed of globules and strands of loose fibrin, polynuclear leucocytes, exfoliated epithelium, and serous fluid. The walls of the vesicles are, in places, thickened by many spindle cells, and the capillaries are deficient. Some vesicles are partly obliterated by the thickened walls. In other places the vesicles are dilated and filled with exudate. There is no organization of the exudate. The walls of bronchioles are edematous and infiltrated with a few round cells. The pleura is much thickened by a layer of granulation tissue which extends well into the fibrinous exudate. Sections of the pericardium present the same appearance. Gram's stain shows many encapsulated diplococci in the pleura and a few throughout the lung.

There was, therefore, a condition of chronic unresolved pneumonia, due probably to pneumococcus infection. The inflammation extended slightly to the other lung, to the pericardium, mediastinum, under surface of diaphragm, and slightly to the spleen. The dyspnea was fully explained by the persistent pneumonia and pleurisy, and especially by the pericarditis, and

the feeble circulation was evidenced by the well-marked changes of chronic congestion of the liver.

The emaciation and failure of nutrition antedated the pneumonia and must be referred to other factors. The extensive renal lesions failed to yield any of the urinary, circulatory, or toxic signs of Bright's disease, but there may be found reasons for supposing that they contributed essentially to the general failure of nutrition. Other factors leading to the same result are found in the stomach and thyroid gland. The gastric mucosa was everywhere reduced to about one-half its normal thickness, the peptic glands were represented by very short tubes very deficient in acid cells, and the muscularis was unusually thin. There was very little new connective tissue in the mucosa. Little attention is commonly paid to the atrophic thyroid often found in elderly subjects, but it is clear that an extremely fibrous and atrophic thyroid must signify deficient capacity to metabolize nitrogenous food, a defect which was very notable in this patient. The parathyroids were also atrophic and its cells resembled small lymphocytes. The atrophy of the kidneys may perhaps be correlated with the atrophic thyroid and both together with the gastric atrophy may account for the emaciation and failure to maintain the nutrition of protein tissues.

A curious relation existed between the adrenal and pancreas which is of interest in connection with the theories regarding the metabolic functions of these organs. The adrenals were enormously hypertrophied, measuring 7 x 4 x 1.5 cm., and contained a corresponding excess of chromaffine cells. One may suppose that this condition indicated an unusual capacity to metabolize carbohydrates. In the pancreas there was extensive reduction of alveoli devoted to external secretion, while the islands of Langerhans were increased in number and size. This condition may indicate increased capacity to burn carbohydrates. As a matter of fact, during the last two years the patient lived chiefly on carbohydrates and showed a marked repugnance toward meats.

In a patient whose failing nutrition seems to have depended on such marked changes in stomach, kidneys, thyroid, pancreas,

and adrenals it is perhaps not a matter of surprise that a complicating pneumonia should fail to resolve, especially if, as it is said, immunity is ultimately a function of the organs.

A diagnosis of syphilis was made by several of the many consultants in this case. Aside from the ocular lesion, which failed to show spirochetes or the definite histological signs of syphilis, there were none of the organic lesions upon which one depends for the anatomical diagnosis of late syphilis. Levaditi stains of many tissues were all negative.

It has long been known that many cases of adhesive pericarditis and mediastinitis are associated with chronic pleurisy and followed by chronic peritonitis, swelling of the liver, and ascites, constituting a condition often called polyserositis. This condition has been described especially by Romberg,[1] Pick,[2] Hess,[3] and others, but the exact etiology and pathogenesis of the condition have not been made clear. Recently Schlayer,[4] in Romberg's clinic, has expressed the opinion that the disease is essentially an inflammatory process which extends from pleura, pericardium, and mediastinum to the liver and peritoneum, and that stasis from heart weakness has little to do with the severe inflammations and exudates. The present case resembles some of those reported by Schlayer, and since in this instance the etiology and course of events starting from the pneumonia are quite clear the observations may have some bearing on the nature of more chronic and typical cases of Romberg's disease in which the relation to previous acute pleurisy or pneumonia is not apparent.

REFERENCES.

[1]ROMBERG: Lehrb. d. Krankh. d. Herzens u. d. Gefässe.
[2]PICK: Ztschr. f. klin. Med., 1896, xxix, 385.
[3]HESS: Uber Stauung. u. chron. Entzund. in d. Leber. Marburg, 1902.
[4]SCHLAYER: München. med. Wchnschr., 1910, lvii, 729.

Discussion.

DR. CHARLES NORRIS asked where the unresolved pneumonia was—in the upper or lower lobe. He had understood Dr.

Ewing to say that the patient had had an adhesive pericarditis. Was this really a lung in which the formation of connective tissue took place?

Dr. RICHARD M. PEARCE had understood that there was really no organizing pneumonia in the lung. There was simply the history of pneumonia without resolution. He asked whether it was justifiable to assume that an acute inflammatory condition was constantly present in the lung during the entire fourteen months. Might it not be possible that the individual had had recurrent attacks of pneumonia?

Dr. W. G. MacCALLUM asked whether there was any record of the patient's blood pressure.

Dr. EWING said that the location of the pneumonia was chiefly in the right lower lobe; to some extent in the upper; the other lung was slightly affected. The pericarditis was dry with contraction, and the heart was small, so that there was no pressure on the heart. Regarding the identity of the condition found at autopsy with that giving the acute symptoms in the beginning of the illness, it was concluded that the condition of the lungs at death was representative of and the direct result of the condition established at the time of the acute attack, principally on account of the clinical history, which showed continuation of the auscultatory signs at the exact point of attack. An exacerbation might have occurred just before death, but was strongly contraindicated by the history. There was nothing in the clinical history to indicate a terminal pneumonia. There was no organization of the exudate. There was some thickening of the walls of the vesicles which would be likely to accompany a prolonged process of this sort. There were no determinations of the patient's blood pressure. The pulse was not of high tension, and there was not the slightest suspicion that the patient has such extensive disease of the kidneys. There was very slight arteriosclerosis.

Dr. NORRIS suggested the possibility that this might be a case of aspiration pneumonia. He questioned the possibility of an acute pneumonia lasting for fourteen months.

Dr. Ewing thought that Dr. Norris would agree, after he had examined the specimens and the sections under the microscope, that there was not the slightest ground for the suggestion of aspiration pneumonia. He would repeat that the patient had been a source of great interest to many prominent clinicians for a long period. There was nothing lacking in the clinical observation, and he was, therefore, able to offer these clinical data with some assurance.

Dr. Norris thought that most of the aspiration pneumonias were never diagnosed by the clinicians, and that many cases of Bright's disease were also not diagnosed during life.

THE BACILLUS OF RHINOSCLEROMA.

WILLIAM C. THRO, M.D.

The organism here described was obtained from an individual under the care of Dr. C. G. Coakley. The histological diagnosis of rhinoscleroma was made by Dr. W. J. Elser, who suggested that the organism be studied and that treatment by vaccination might be beneficial.

Clinical History.—The patient, a Russian, thirty-five years of age, male, has lived in the United States for fifteen years. The nodal lesion was first discovered four years ago by a surgeon who was treating him for deafness. At the present time it is confined to the nose, which is slightly enlarged externally, with partial occlusion of the left nares and almost entire obliteration of the right.

Sections from the mass show the characteristic structure of rhinoscleroma, and in the hyaline areas the encapsulated bacilli, supposed to be the etiological factor, were found.

From a study of the literature it is evident that there are different strains of the bacillus of rhinoscleroma. For example, Paltauf states that it coagulates milk; Abel that it does not.

Some strains produce gas with saccharose, and others do not. The strain isolated from this case grows in cultures as diplococci, or short or long rods, singly or in chains. The organism has a large, well-developed capsule similar to *B. mucosus capsulatus*. It is non-motile and Gram-negative. At 37° C. it grows luxuriantly in all the media tested and it lives for months at room temperature.

The growth in various media will be compared with that of three strains of *B. mucosus capsulatus*, one from an abscess, designated "Elser"; one from a case of pneumonia, designated "Shea"; and one from a case of chronic bronchitis, designated "Guide."

Broth.—All three organisms clouded the broth uniformly, with the formation of a ring at the surface of the media, and an abundant white sediment. The bacillus of rhinoscleroma occurred in broth in long chains of encapsulated rods.

Agar.—On the original plates (isolated December 18, 1909) the surface colonies of *B. rhinoscleromatis* were 1 millimeter in diameter after twenty-two hours, whitish, opaque, and circular, with irregular edges. The deep colonies were similar except that they were more transparent and died out sooner. When touched with a loop the growth could be drawn out to a distance of 1 cm., which is a well-known characteristic of *B. mucosus capsulatus*. On slant agar, the growth is abundant, thick, shiny, spreading, and whitish.

Milk.—*B. rhinoscleromatis* and two strains of *B. mucosus capsulatus* did not coagulate the milk, while one strain of the latter did.

Potato.—On potato *B. rhinoscleromatis* grew very sparsely, and in this respect differed from the strains of *B. mucosus capsulatus* which produced an abundant growth in twenty-four hours resembling, on the upper portion of the potato, clumps of small white beads.

Dunham's Peptone Solution.—*B. rhinoscleromatis* and all the strains of *B. mucosus capsulatus* produced a slight cloudiness of the peptone solution, and all gave a faint indol reaction.

Hiss' Serum Inulin.—None of the strains coagulated this medium at the end of five days.

Gelatin.—None of the strains liquefied gelatin. At the end of twenty-four hours *B. rhinoscleromatis* had grown only one-half the length of the stab, but ultimately it grew the full length, as did also the strains of *B. mucosus capsulatus.*

Carbohydrates.—The sugar-free agar and broth were made up according to directions given by Elser and Huntoon.[1] Merck's dextrose, levulose, saccharose, lactose, maltose, mannit, galactose, dextrin, inulin, and dulcite were used. In inoculating the agar the straight wire was drawn along the slant and the medium was then stabbed. At the end of twenty-four hours *B. rhinoscleromatis* caused a faintly acid reaction in the agar containing dextrose, levulose, mannit, and galactose, and at the end of forty-eight hours the maltose medium was also acid. At the end of several weeks an acid reaction was obtained with all the carbohydrates except lactose, dextrin, inulin, and dulcite, which were alkaline. With mannit and inulin the lower portion of the agar ultimately became decolorized. The reaction of the different strains and the changes taking place are shown in the table.

In the fermentation tubes *B. rhinoscleromatis* never produced gas by the end of thirty days. The closed arm became clouded with all except lactose, dextrose, and dulcite media.

None of the strains of *B. mucosus capsulatus* produced gas in inulin, dulcite, or dextrin media. One, however, produced gas in the other media, though very slowly in saccharose. Another strain differed from the preceding in the non-production of gas in lactose, while a third strain of *B. mucosus capsulatus* did not produce gas in lactose and produced only a bubble of gas in saccharose and maltose. The reaction of the media in the bulbs changed from day to day.

Agglutination.—The chief object in isolating the organism from this patient was to try the effect of vaccine therapy. Before the first injection of vaccine the patient's serum was tested

[1] ELSER AND HUNTOON: Studies on Meningitis, *Jour. Med. Research,* 1909, xx, 375.

TABLE I.——CULTURAL CHARACTERS

NAME OF CULTURE	BROTH	MILK	GELATIN	POTATO	HISS' SERUM INULIN	INDOL DUNHAM'S PEPTONE
B. rhinoscleromatis	Cloudy Much sediment	Not coagulated	Not liquified Nail-like	Slight growth	Not coagulated	Faint trace
B. mucosus capsulatus "ELSER"	Uniformly cloudy Distinct ring at top of media	Coagulated	Not liquified Nail-like	Good growth Raised, pale, yellow, shiny	Not coagulated	Faint trace
B. mucosus capsulatus "SHEA"	Uniformly cloudy Ring at top of media	Not coagulated	Not liquified Nail-like	Good growth Raised, shiny, granular	Not coagulated	Faint trace
B. mucosus capsulatus "GUIDE"	Uniformly cloudy Ring at top of media	Not coagulated	Not liquified	Good growth Raised, shiny, granular	Not coagulated	Faint trace

Table II.——CARBOHYD

NAME OF CULTURE	DEXTROSE			LEVULOSE			SACCHAROSE			LACT	
	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb
B. rhinoscleromatis	0	Ac	+	0	Ac	+	0	Ac	+	0	Alk
B. mucosus capsulatus "ELSER"	.66	Ac	+	.56	Alk	+	.35	Alk	+	.58	Ac
B. mucosus capsulatus "SHEA"	.50	3d Ac	+	.70	3d Alk	+	.25	3d Alk	+	0	3d All
B. mucosus capsulatus "GUIDE,"	.13	Ac	+	.13	Ac	+	.01	Ac	+	0	All

NAME OF CULTURE	DEXTROSE			LEVULOSE			SACCHAROSE			LACT	
	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days
B. rhinoscleromatis	Ac	R	R	Ac	R	R	N	B R	B R	N	R
B. mucosus capsulatus "ELSER"	Ac	R Y	R	Ac	R	R	Ac	B R Y	B Y	Ac	R Y
B. mucosus capsulatus "SHEA"	Ac	B Y	B Y	Ac	R Y	B Y	Ac	B Y	B Y	Alk	Y Y Y
B. mucosus capsulatus "GUIDE"	Ac	R Y	R	Ac	R	R	Ac	R Y R	R	Ac	Y R

Ac—*Acid.*   Alk—*Alkaline.*   N—*Neutral.*   R—*Red.*   Y

The decimals refer to the proportion of the closed arm filled w

Cloud in Closed Arm	MANNIT			GALACTOSE			DEXTRIN			INULIN			DULCITE		
	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm	Gas in Closed Arm	Reaction of Bulb	Cloud in Closed Arm
+	0	Ac	+	0	Ac	+	0	Alk	0	0	Alk	+	0	Alk	
+	.83	Alk	+	.71	Ac	+	0	Alk	+	0	Alk	+	0		+
+	.35	3d Ac	+	.50	3d Ac	+	0	3d Alk	+	0	3d Alk	+	0	3d Alk	0
+	.52	Ac	+	.25	Ac	+	0	Alk	0	0	Alk	+	0	Alk	0

MUS AGAR

Color Media, 40 days	MANNIT			GALACTOSE			DEXTRIN			INULIN			DULCITE		
Reaction, 1 day	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days	Reaction, 1 day	Color Med., 14-30 days	Color Media, 40 days
R	Ac	B/Y	B	Ac	R	B/R	N	B	B	N	B/Y	B/Y	N	B/N	B/N
<	Ac	B/Y	B/Y	Ac	R/Y	R/Y	Ac	B/Y	B/Y	N	B/Y	B/Y	N	B	B
<	Ac	B/Y	B/Y	Ac	B/Y	B/Y	Alk	B/Y/R	B/Y	Alk	B/Y/N	B/Y	Alk	B/N	B
<	Ac	R/Y	B/Y	Ac	R/Y/R	R/Y	Alk	B/V/N	B/Y	Alk	B/Y	B	Alk	B/N	B/Y

B *Blue or Alkaline.*

for agglutinins in dilutions varying from 1 to 10 to 1 to 50. The results were negative. After treatment for one month the serum was again tested with similar results.

Treatment.—The bacteria used for vaccination were heated at 65° to 70° C. for one hour. All the injections were given subcutaneously in the arm. The patient was weighed frequently, and there was no great variation. After some injections there were slight redness and pain at the site of the injection, and several times the patient had attacks of epistaxis and tenderness of the nose on pressure.

The results are negative, since there has been no change in the size of the growth, although the patient states that he can breathe much more easily.

The dosage of the vaccines was as follows:

Jan. 11.— 15 millions.	Mar. 19.—132 millions.
" 15.— 20 "	" 22.—144 "
" 18.— 25 "	" 26.—165 "
" 22.— 35 "	" 29.—198 "
" 25.— 45 "	Apr. 2.—264 "
" 29.— 45 "	" 5.—330 "
Feb. 8.— 60 "	" 12.—528 "
" 15.— 60 "	" 19.—594 "
" 19.— 65 "	" 26.—574 "
" 22.— 65 "	May 2.—528 "
" 26.— 75 "	" 12.—600 "
Mar. 1.—105 "	" 19.—637 "
" 5.— 97 "	" 24.—637 "
" 8.— 97 "	" 31.—637 "
" 12.—112 "	

Discussion.

DR. F. S. MANDLEBAUM had had the good fortune to examine material from four cases of rhinoscleroma. The first two cases were typical ones and occurred some ten or twelve years ago. Four years ago a young woman of sixteen had presented herself at the out-patient department of Mt. Sinai Hospital with a lesion of the larynx and trachea. A small portion of the larynx was excised and sent to the laboratory for diagnosis. Remembering the picture of the slides in the earlier cases, Dr. Mandlebaum was able to make a diagnosis of scleroma. This case was the first in this country of primary scleroma of the trachea and pharynx. The Mikulicz' bodies were found in great profusion and the smaller ones were filled with the bacilli. The larger cells showed the bacilli scattered at the periphery, and this was apparently caused by a mucoid degeneration or some product of secretion from the capsules of these organisms. These cells and their bacilli stained with the ordinary basic anilin dyes as well as with hematoxylin, and could be readily seen. The hyalin bodies showed some rather peculiar features; they formed distinct rosettes with a sort of nuclear substance usually found in the central portion; and they were very symmetrical. At times some of the hyalin material did not stain well. The Gram stain proved to be the best for bringing out the hyalin body, but it also stained well with acid stains, such as eosin or picric acid. Dr. Mandlebaum showed photomicrographs made at the time he had studied the case, one of low power showing the Mikulicz' cells rather well filled with bacilli. The higher power, 1000 diameters, showed one of the large cells in which the bacilli were seen only at the periphery. Occasionally some bacilli were seen in the tissues about the cells. Other photographs were made simply to show the hyalin body present in large numbers and the rosette forms. The first sections were stained with polychrome methylene blue which seemed to be the very best of all staining agents for the purpose. Cultures were made from this case; and an organism was grown which was practically identical with Friedländer's bacillus.

ADENOMYOMA OF THE FALLOPIAN TUBE.

W. G. MAC CALLUM, M.D.

The case was one operated upon at the German Hospital by Dr. Seeligman for the extirpation of a myomatous uterus in which enlargements of the Fallopian tubes were found as an accidental discovery. On one side there was a small nodule situated about one centimeter from the cornu of the uterus—on the other side the proximal part of the tube was of normal size, while an enlargement of considerable size occupied the middle portion extending toward the fimbriated extremity. This mass measured 25 cm. in diameter and was irregular and nodular in form. Transverse sections through the small nodule on the left side showed several lumina. On the right side accessory lumina appeared in the apparently normal portion of the tube between the cornu and the large nodule. Section through the nodule itself revealed a number of cyst-like cavities filled with a brown turbid fluid. These are seen to be lined with a cubical or columnar epithelium and to be associated with numerous micro-scopic masses of gland-like or tubular spaces lined with similar epithelium and quite separate from whatever may represent the original lumen of the tube. In association with these new formations there is a great excess of smooth muscle tissue.

It seems clear that this is an example of the adenomyoma of the Fallopian tube, such as has been described by von Recklinghausen, Emil Ries and others.

Von Recklinghausen explained their origin by considering them the result of the development of remnants of the Wolffian duct which runs in intimate relation with the uterus, crossing the Fallopian tube near the cornu, while others, such as Ries and Cullen, think it more probable that the epithelial lined cavities arise from the epithelium of the mucosa of the tube or of the uterus, either as a result of displacement or as the remote effect of distorting inflammatory processes.

In this instance there is no evidence of even the remnants

of an inflammatory process and the case was, therefore, re-
garded as a true adenomyoma developing in the tube.

In spite of the counter evidence there still seems to be much
to be said in favor of von Recklinghausen's theory.

AN UNUSUAL LESION OF THE LARGE INTESTINE.

S. R. BLATTEIS, M.D.

History.—D. J., aged thirty-four, admitted to the Jewish
Hospital, of Brooklyn, in the service of Dr. William Linder on
April 5, 1910, a native of Warsaw, Russia. Family history
negative. Patient had the usual diseases of childhood; has been
six years in this country; is a tailor by occupation; is married
and has had five children, three of whom are living; one died of
diphtheria, the other of measles. He smokes and drinks moder-
ately; denies venereal disease. Never had a doctor since child-
hood until December 15, 1909, when, while in apparent good
health, he was seized with severe abdominal cramps which lasted
intermittently through the night and the following morning. His
case was then diagnosed as appendicitis, and operation was ad-
vised. As his condition somewhat improved, this was refused.

From that time until the time of operation, April 15, 1910
(four months), the patient suffered from numerous attacks of
abdominal pain that were distinctly referable to the right iliac
fossa. From the first attack until the day of operation he suf-
fered from attacks of indigestion and a great deal of flatulence,
complaining of annoying gurglings in the right iliac fossa. His
appetite was fair; he never vomited, was very constipated, gradu-
ally failed in health and became thinner and very anemic.

The urine and feces were normal. The blood count on
April 6, nine days before the operation, was as follows: Total
leucocytes, 11,200; polymorphonuclears, 68 per cent.; small and
large lymphocytes, 28 per cent.; mononuclears and transitionals,

3.5 per cent.; eosinophiles, 0.5 per cent. For nine days before the operation his temperature varied from 98.6° to 100.6°. An x-ray examination showed nothing. The Wassermann reaction was negative.

The post-operative history can be summed up in the statement that "the patient is making an uneventful recovery." All the pain has disappeared and his bowels have a normal daily evacuation.

Gross Description of Specimen.—The resected intestine measures 37 cm. and consists of 5 cm. of the ileum, the appendix, the cecum, the ascending colon, and the beginning of the transverse colon. With the exception of 6 cm. of the end of the transverse portion, the specimen shows the following:

The wall of the intestine is markedly thickened and edematous, varying in thickness from 1.5 cm. at the cecum to 2 cm. at some portions of the ascending colon, the thinnest portion being from 3 to 5 mm. This thickening is confined almost exclusively to the submucosa, there being but slight thickening of the muscularis.

Macroscopically, the submucosa appears to be honeycombed, very strongly resembling tissue after infection with the *B. aerogenes capsulatus;* these cystic chambers vary in size from 1 to 3 mm. in diameter and are irregular in shape. As a result of this swelling of the intestinal wall, the mucous membrane is thrown into numerous thick folds; there are also evidences of varying degrees of inflammation. The mucous membrane is covered with a thick tenacious mucus.

The appendix is 6 cm. long, is of the usual thickness, and does not show the changes described in the intestine. Attached to the intestine is the greater part of the ascending mesocolon. Along the mesentery of the ileo-cecal portion are a number of enlarged lymph nodes varying in size from 0.5 to 1 cm. on cross section. These glands, except for their size, show no abnormal appearance.

Three pieces of the intestine were submitted for examina-

tion, one from the central portion, and one from each end of the resected intestine.

Pathological Examination.—Intestine.—The lesions are essentially alike in all portions of the specimen. The characteristic lesion is in the submucous coat and consists in the extreme dilatation of the lymphatic vessels, in consequence of which this coat is much swollen and presents to the naked eye a honey-combed appearance, due to the presence of numerous cystic spaces, with intervening, often thin septa of connective tissue. These spaces are present throughout the submucosa, but tend to be rather larger and closer together in the internal part than in the part near the muscular coat.

While there is a uniform swelling of the submucosa, this swelling is greater in some places, so that these project further toward the lumen of the intestine. The cysts vary in size and shape; some are round or oval; others are irregular in shape, with thin septa crossing them or extending only into their lumina. There are evidences of the coalescence of the cystic spaces by atrophy of the adjacent septa. Many of the cavities are empty; others contain a finely granular material; still others contain fibrin and leucocytes or masses of leucocytes. Most of the cavities are lined with a single layer of endothelium; some are lined with several layers of proliferating endothelium.

The leucocytes within the dilated lymphatics are of both the polynuclear and the lymphocytic types, including plasma cells and also eosinophiles. Polymorphonuclear leucocytes are numerous, many of these being eosinophilic. A conspicuous feature of the lesion is the presence within the dilated spaces of large numbers of giant cells with central multiple nuclei. In some instances these almost completely fill up the spaces, and in others are arranged so as to form their inner lining. These cells, in the main, resemble foreign body giant cells.

The intervening stroma is connective tissue which in a few places is densely fibrous, but in most places is edematous and richly infiltrated with cells. Proliferating connective tissue cells are seen, but the predominant cells in the meshes of the edema-

tous tissue are leucocytes, both mononuclear and polynuclear, and not infrequently eosinophilic. There are places, especially near the muscularis mucosæ, where the leucocytes are densely packed and are undergoing necrosis with extensive nuclear fragmentation. Delicately fibrillated fibrin is abundant, although not uniformly present in the meshes of the connective tissue of the submucous coat. The solitary follicles appear essentially normal, perhaps in some instances moderately swollen. The mucous membrane is intact. The cells of Lieberkühn's glands are well preserved and are mostly calyciform. The lymphatic tissue of the mucosa appears essentially normal. The lymphatics of the mucosa, if dilated at all, are only moderately so, and do not show cystic dilatation as in the submucosa. The main muscular coat is moderately infiltrated with wandering leucocytes, but is otherwise normal, as is the peritoneum.

Lymphatic Gland.—Here the principal lesion is the presence in the lymph sinuses of large cells of an endothelial type, which are probably the result of proliferation of the reticulum cells. The general architecture of the gland, with distinction between follicular substance and sinuses is preserved. This condition is the so-called irritative hyperplasia of lymphatic nodes, and is not of especial significance.

Diagnosis.—Lymphangiectasia cavernosa of the intestinal submucosa, with inflammation and hyperplasia of the same coat. Irritative hyperplasia of the mesenteric lymphatic nodes.

The wide extent of the dilatation of the submucous lymphatic vessels is most remarkable. No positive evidence of the formation of new lymphatic vessels is apparent, so that the case is interpreted as dilatation of the pre-existent lymphatics of the submucous coat of the intestine. The cause of the lymphangiectasis is not apparent in the sections. Nor can a definite statement be made concerning the contents of most of the larger cyst-like spaces. In the sections these are empty. As already stated, some coagulated lymph and fibrillated fibrin can be seen in some of the spaces, and in others, especially the smaller ones,

there are many leucocytes; but, unfortunately, the sections do not show the contents of the larger spaces.

Discussion.

Dr. W. G. MacCallum had seen the sections in Baltimore, at the time that Dr. Welch examined them. The point of greatest interest was the nature of the contents of these cavities and of the walls of the cavities themselves. He had not been able to convince himself that all the cavities represented lymph channels. It would be interesting to know what bacteria were found.

Dr. Blatteis said that no definite organism was present in any of these spaces.

Dr. MacCallum thought that the inflammatory reaction suggested the possibility that there were organisms present. He would like to know whether there had been any gas present in the cavities, which could not be determined by mere microscopic inspection. He had tried unsuccessfully to elicit crepitation in the specimen presented. He had also seen the case to which Dr. Whipple had referred, that of a student who had lived for some years in Turkey; but he saw no points of resemblance in the two cases. In Dr. Whipple's case there was a very remarkable deposit of fat and fatty acids in various places in the mesenteric glands and elsewhere.. The suggestion was made by Dr. Whipple largely on account of the presence of fat, and it seemed possible that fatty acids might have been extracted in this case.

Dr. Eli Moschcowitz said that within the past day or two he had dissected a case in which a similar picture was found in the wall of the stomach. As yet no sections had been made, but macroscopically the lesion appeared identical with that presented by Dr. Blatteis. The specimen occurred in a patient who had carcinoma of the head of the pancreas. The gastro-hepatic omentum was densely infiltrated with carcinoma and the glands along the lesser curvature were the seat of large metastases. Especially significant was the fact that the honey-combing of the submucosa was particularly prominent in the neighborhood

of the lesser curvature, becoming less and less marked toward the greater curvature. He thought that the condition was probably a lymphangiectasis due to obstruction of distal lymphatics, and he suggested that in Dr. Blatteis' case there was a lymphatic obstruction in the mesentery, corresponding to the drainage area of the affected part of the colon, which in all probability would eventually reveal itself.

DR. O. H. SCHULTZE was reminded of a case of phlegmonous gastritis which he had seen several years ago. The description was not definite as to whether this case was really a lymphangiectasis. Were these cavities definitely lined with epithelial cells? The question of the bacteria present was important.

DR. JAMES EWING suggested that the investigation of this case should include the mesentery and other portions of the intestinal wall. He had examined the sections with care and interest. The description given was clear, except that in the sections which he had looked at the spaces were usually lined by giant cells of the foreign body type, such as appear in inflamed fat tissue. He thought he had detected traces of fecal matter in some spaces. He would suggest that the condition had resulted from inflammation and degeneration of the submucous fat tissue.

DR. BLATTEIS said that there was no crepitation in the fresh specimen. The spaces were apparently empty, at least they were macroscopically empty. No definite contents could be determined—cystic, fecal, or otherwise. There was apparently no obstruction anywhere higher up. The clinical history was against the suggestion of a phlegmonous inflammation; the temperature of the patient never exceeded 100.6°, and the patient recovered.

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Dr. Richard M. Pearce, *President.*

A NEW METHOD FOR THE ESTIMATION OF CRANIAL CAPACITY AT AUTOPSY.

BY A. J. ROSANOFF, M.D., AND JOHN I. WISEMAN, M.D.

It has been shown by the researches of Bartels,[1] Pfleger,[2] Bolton,[3] Mittenzweig,[4] Southard,[5] Watson,[6] and many others that the average weight of brains of insane subjects is below the normal average; and it has also been shown that when cases of idiocy and imbecility, epilepsy, general paresis, and coarse cerebral lesions are excluded from consideration, the average is still found to be below the normal.

The questions that at once suggest themselves are: How often and in what clinical types of cases is this reduction in weight due to a process of atrophy? How often does it constitute an original defect?

In this paper we purpose to discuss: (1) the methods that are generally employed for the detection of atrophy; (2) existing methods for the estimation of cranial capacity; and (3) a new method proposed by us.

1. *Methods Generally Employed for the Detection of Atrophy.*

Within the past four years one of us has had occasion to examine a very large number of post-mortem records in five large hospitals for the insane in this State and in five large general hospitals in New York and in Boston. The only points that were found to be recorded as having a bearing upon the question of brain atrophy were brain weight; certain gross appearances, such as shrinkage of gyri, widening of sulci, and excess of cerebrospinal fluid; and certain microscopical appearances. A review of the literature pertaining to this subject has also shown that with some few exceptions—notably the recent work of Reichardt[7] —no attempt has been made to apply more accurate methods even in special investigations.

The fact that brain weight varies normally within wide limits renders the record of such weight alone in a given case of but little value. For it is obvious that a brain may be found at autopsy to be as high as the normal average in weight, or even higher, and yet may be one in which atrophy to the extent of 200 grams has occurred. And it is equally obvious that a brain may weigh 200 grams less than the normal average and yet may be one in which no atrophy has occurred.

Estimation of degree of atrophy from gross appearances, such as shrinkage of gyri and widening of sulci, is at best but roughly approximate, there being no way of taking exact measurements. Indeed, when the atrophy is but slight or moderate, as it is in most cases, its very existence may escape detection if judgment is based on these gross appearances.

Increase of cerebrospinal fluid as a measure of atrophy also has sources of large error. In the first place it is difficult to drain and collect all the fluid from the subdural and subarachnoid spaces and from the ventricles; in the second place it is difficult to prevent an admixture of blood and serum from the severed blood vessels; in the third place there is no way of judging what proportion of the fluid is derived from the cranial cavity and what proportion from the spinal canal; and in the fourth place encroachments upon the cranial cavity resulting from thickening of the dura, formation of false membranes due to pachymeningitis, etc., would fail to be taken into account.

It would seem safe to say, without going into an extended discussion, that microscopical methods are still less helpful than the methods already discussed in estimating degree of atrophy.

In the meantime, parallel with the anatomical observations showing that the average weight of brains of insane subjects is below the normal average, there are gradually accumulating clinical observations showing, on the one hand, that insanity is most apt to develop in persons of inferior or at least vulnerable mental make-up, and on the other hand, that most forms of insanity gradually lead to functional deterioration.[8]

These considerations have directed our interest to the development of a convenient method by means of which atrophy, even when present in but slight degree, can be detected, so that cases of low brain weight resulting from atrophy may be distinguished from those due to original defect.

Assuming that there is some correspondence between cranial capacity and brain weight, and that the ratio representing this correspondence can vary normally only within narrow limits, we sought to develop a practical method for the estimation of cranial capacity, since cranial capacity seems to be the only available criterion of judgment as to the original weight of the brain in any given case.

Our plan is to find by means of a large number of measurements the normal ratio between cranial capacity and brain weight. Any increase of this ratio in a given case would indicate abnormal reduction of the brain mass, which, in the absence of evidences of compression, would be attributable to atrophy.

2. *Existing Methods for the Estimation of Cranial Capacity.*

The methods that have been proposed for the estimation of cranial capacity depend upon the employment as filling material either of metallic shot, glass beads, or peas, or of liquids, principally metallic mercury and water.

As between shot, beads, and peas, beads are preferred, shot being heavy and peas having the disadvantage of swelling from contact with moisture and shrinking again on being dried, therefore giving inconstant results.

Glass beads are quite suitable and under certain conditions capable of furnishing reliable results. Thus in a series of one hundred estimations made in Prof. von Török's[9] laboratory by Kelemen the maximum error was a trifle over 1.5 per cent. In this series of estimations a bronze model of a skull, the same selected lot of beads, and the same measuring cylinder were used throughout. These conditions, however, are not like those under which at most autopsies estimations of cranial capacity must be made. It would seem that if this method were generally adopted the extent and frequency of error would inevitably be much greater than in the case of Kelemen working under artificial and strictly uniform conditions. The slightest irregularity in the shape of the beads, a lack of uniformity in their size, failure to use a measuring cylinder of exactly the same shape and size in every estimation would very materially affect the accuracy of the method.

As regards methods which depend upon the use of liquids as filling material, we fully agree with von Török who considers them all, with possibly one exception which we shall refer to later, as entirely untrustworthy. Yet quite recently Reichardt has again suggested such a method. He insists upon a very straight saw cut, upon estimating the cranial capacity before sectioning the thorax and abdomen, and upon repeating the estimation in each case at least ten times, disregarding the results obtained in the first three or four estimations, and using only the calculated average of the results of the last six or seven estimations.

Reichardt himself points out some of the sources of error. Thus he states: "Our investigations have taught us that even slight irregularities of the saw cut may cause an error to the extent of minus 300 c. c." He states also that leakage into the foramen magnum, the smaller basal foramina, and the large blood vessels may cause great error, to obviate which he recommends pouring water into the base of the skull until the level at these points of leakage remains constant for several minutes. In some cases, he states, it may be necessary to use corks, putty, or non-absorbent cotton for sealing up the points of leakage.

There are still other sources of error which Reichardt does not mention. Failure to insure a perfectly horizontal position of the level of the saw cut in filling either the base or the calvarium would necessarily involve great error, for it must be remembered that the circumference of the skull is so wide that a difference of 1 mm. in depth of the water makes a difference of about 30 c.c. in the reading.

It must be noted, however, that Reichardt does not claim for his method absolute accuracy. He maintains merely that with the exercise of some care the error involved in the use of his method may be reduced to within 50 c.c., and he maintains further that an error of such degree would not affect the practical usefulness of his method. The latter assumption we believe to be untenable, for all available data show that importance attaches precisely to the slighter reductions in the brain weight, so far as the functional insanities are concerned, the coarser reductions being observed mainly in connection with arrests of development and with organic brain lesions.

We have still to consider another method which has been devised by Poll.[19] The essential feature of this method consists in the use of a bag, made of very thin rubber, which is placed in the cranial cavity and through a trephine opening filled with water. The rubber is so extensible that it is supposed that the mere weight of the water is sufficient to cause the bag to bulge so as to fill every irregularity in the cranial cavity. Poll and later von Luschan have obtained by the use of this method results

with error of less than 1 per cent. By an ingenius experiment von Török has shown that it is very difficult, if at all possible, to make the bag actually fill every irregularity in the cranial cavity. He covered the inside of a dry skull with sticky colored crayon; then in testing Poll's method he found that the rubber bag failed in many spots to get an impression of the crayon, showing that at those spots it did not come in contact with the skull bones.

Aside from the possible inaccuracy of Poll's method, its inconvenience and the difficulty of obtaining the necessary rubber apparatus—which does not appear to be on the market—would render that method unsuitable for common use, and therefore not likely to be generally adopted.

It seemed to us, therefore, that there was still a need for a simple yet sufficiently accurate method for estimating cranial capacity.

3. Description of the New Method.

The special feature of our method consists in the use of putty as filling material. The details of technique are as follows.

No special care needs to be exercised in opening the skull; it is necessary to guard only against extensive cracking or chipping out of large fragments of bone. The angular or so-called undertaker's saw cut is to be preferred to the circular one. The dura is incised and the brain removed in the usual manner. The dura is then carefully stripped from the base of the skull and cut away by a circular incision made as far below the foramen magnum as possible. The foramen magnum is now closed by means of a cork stopper of suitable size pressed down until its upper edge no longer protrudes above the internal surface of the occipital bone but is on the same level with it. The base of the skull is then filled with putty, small lumps being used at first which are carefully pressed in so as to fill all the irregularities. The calvarium is filled with putty in a similar manner, after which it is replaced and by pressure part of the excess of putty is squeezed out through the saw cut. The next step is to fit the calvarium over the base of the skull as exactly as possible and

here slight irregularities and angles in the saw cut are very helpful. The final fitting is most readily accomplished by gentle tapping with a wooden or rawhide mallet upon the top of the skull and carefully removing the excess of putty as it appears through the saw cut.

The putty as used for this purpose must be much softer in consistency than as used ordinarily by glaziers. It may readily be softened by being kneaded with linseed oil, and if too soft it may be made firmer again by the addition of whiting.

The putty is best kept under water; this prevents it from drying and renders it unnecessary to soften it afresh every time that it has to be used.

It is advisable to keep the hands wet with water to prevent the putty from sticking to them. Generally the moisture which covers the inside of the skull prevents the putty from sticking to the skull bones. Sometimes it does stick slightly in places, but it can always be easily and completely removed.

We use for measurement two glass cylinders of 2,000 c.c. and 1,000 c.c. capacity respectively. The smaller cylinder is filled with water exactly up to the 1,000 c.c. mark. About 200 c.c. is then poured over into the larger cylinder. The putty from the cranial cavity is then put into the large cylinder preferably in small lumps rolled up and allowed to slide down slowly by inclining the cylinder to prevent splashing of the water. After all the putty has been put into the cylinder and gently pressed down with a stick, more water is poured in from the smaller cylinder until the level is exactly at the 2,000 c.c. mark, care being taken that no bubbles of air are caught underneath or between the lumps of putty. The reading is now taken on the smaller cylinder. By deducting from 2,000 the number of cubic centimeters which were taken from the smaller cylinder to fill the larger one, the figure representing the cranial capacity in cubic centimeters is obtained.

4. *Results Obtained in Twenty Autopsies.*

We present the results obtained in a small number of autop-

sies merely to show that the method is trustworthy and that it reveals evidence of atrophy in cases in which brain weight alone fails to show it.

Our results have been tabulated so as to show in each case the race, sex, age, height, and weight of the subject; the clinical classification; the weight of the brain and that of the dura; the cranial capacity estimated one, two, or three times; and the calculated ratio between cranial capacity and brain weight.

The close correspondence between the results obtained by repeated estimations in the same cases show that the method is trustworthy. In all cases but two, variation of the results was within the limits of less than 1 per cent. In the two cases in which the variation was higher (though still within the limit of less than 50 c.c. regarded by Reichardt as permissible) the discrepancy was ascribed to the fact that in opening the skull the calvarium was badly cracked.

The ratio between cranial capacity and brain weight is shown in our table to be very variable in pathological cases. Its full significance will, however, become apparent only when a large number of observations upon normal as well as insane subjects have been made.

[1]*Neurol. Centralbl.*, 1887, p. 261.
[2]*Jahrb. f. Psychiat.*, Vol. 3, p. 107.
[3]*Jour. Ment. Sci.*, Apr., 1905, p. 20.
[4]*Allg. Ztschr. f. Psychiat.*, 1905, p. 31.
[5]*Am. Jour. of Insan.*, Apr., 1910, p. 673, and July, 1910, p. 119.
[6]*Jour. Ment. Sci.*, Apr., 1910, p. 227.

[7]Ueber die Untersuchung des gesunden und kranken Gehirnes mittels der Wage. Jena, 1906.

[8]Adolf Meyer: An Attempt at Analysis of the Neurotic Constitution. *Am. Jour. of Psychol.*, 1903, p. 90. August Hoch: A Study of the Mental Make-up in the Functional Psychoses. *Jour. Nerv. and Ment. Dis.*, Apr., 1909, p. 230.

[9]Von Török: Ueber ein neueres Verfahren bei Schädel-capacitäts-Messungen, etc. *Virchow's Arch. f. path. Anat.*, 1900, p. 248.

[10]Described by von Török, *loc. cit.*

TABLE SHOWING RESULTS OF TWENTY AUTOPSIES

No.	Name	Color	Sex	Age	Height	Weight	Diagnosis	Weight of Brain	Weight of Dura	Cranial Capacity 1st Estimat'n	2nd Estimat'n	3rd Estimat'n	Cran. Cap. Brain Wt.
273	A. P.	White	M	48	163 cm.	55.79 kgm	Manic-depr. ins.	1517 gm.	84 gm.	1650 c.c.	1643 c.c.	......	1.0857
275	H. D.	Negro	F.	29	149 cm.	......	" "	1317 gm.	43 gm.	1422 c c.	1460 c.c.	......	1.0941
277	J. H. B.	White	M.	57	171 cm.	52.84 kgm	" "	1440 gm.	49 gm.	1620 c.c.	1605 c.c.	......	1.1201
281	J. G.	"	M.	50	171 cm.	58.97 kgm	" "	1500 gm.	69 gm.	1683 c.c.	1690 c.c.	......	1.1247
263	H. G.	Negro	F.	22	148 cm.	78.93 kgm	Dementia praecox	1015 gm.	......	1225 c.c.	......	......	1.2069
274	K. N.	White	F.	68	161 cm.	86.18 kgm	" "	1192 gm.	81 gm.	1340 c.c.	1348 c.c.	1342 c.c.	1.1275
280	L. F.	"	F.	61	155 cm.	......	" "	1265 gm.	67 gm.	1440 c.c.	1437 c.c.	......	1.1375
278	T. B.	"	M.	62	172 cm.	63.96 kgm	Polyneuritic psychosis	1439 gm.	67 gm.	1673 c.c.	1667 c.c.	......	1.1605
267	M. L. U.	"	F.	65	146 cm.	40.37 kgm	Epilepsy	1134 gm.	35 gm.	1200 c.c	......	......	1.0582
272	E. D.	Negro	M.	51	160 cm.	......	Imbecility	1141 gm.	55 gm.	1355 c.c.	1360 c.c.	1350 c.c.	1.1876
279	B. M.	White	F.	90	136 cm.	......	Senile dementia	1010 gm.	40 gm.	1360 c c	1357 c.c.	......	1.3455
283	J. C.	"	M.	71	170 cm.	72.58 kgm	" "	1368 gm.	65 gm.	1590 c.c.	1583 c.c.	......	1.1579
265	J. M.	"	M.	33	160 cm.	45.36 kgm	General paresis	1352 gm.	57 gm.	1555 c.c.	......	......	1.1501
266	S. L.	"	F	39	149 cm.	......	" "	984 gm.	39 gm.	1355 c.c.	......	......	1.3770
268	H. S.	"	M.	59	157 cm.	50.35 kgm	" "	1204 gm.	79 gm.	1515 c c	1577 c.c.	......	1.2583
269	R. M.	"	M.	75	161 cm.	65.32 kgm	" "	1352 gm.	77 gm.	1565 c.c.	1657 c.c.	1645 c c	1.1619
271	L. R.	"	F.	55	161 cm.	......	" "	......	70 gm.	1643 c.c.	1657 c.c.	......	......
284	J. L.	"	M.	56	180 cm.	72.58 kgm	Cerebral softening	1335 gm.	60 gm.	1545 c.c.	1540 c.c.	......	1.1558
282	E. F.	"	F.	75	140 cm.	......	Unclassified	1140 gm.	69 gm.	1397 c.c.	1397 c.c.	......	1.2254
270	J. M.	"	M.	80	155 cm.	79.38 kgm		1307 gm.	......	1527 c.c.	1485 c.c.	......	1.1530

Discussion:

DR. W. G. MacCALLUM was of the opinion that Dr. Rosan-off's method deserved credit for its simplicity and accuracy. He said that he should like to ask Dr. Rosanoff whether he had arrived at a definite idea of how much space is occupied by the dura and blood vessels, and whether the fluid which is accumulated in ordinary cases varied very much under ordinary circumstances, and whether it has to be taken into consideration in this method. Of course, he understood that the method gave the absolute cranial capacity after the dura had been removed.

DR. ROSANOFF replied that his method gave the absolute cranial capacity after the dura had been removed. All of his cases were cases of insanity, but not in all was there any evidence of atrophy. In cases in which there was no evidence of atrophy, the difference between the figures representing the cranial capacity and the figures representing the brain weight, was less than 100. In some cases in which there was very marked atrophy, the figure was above 200, and even much more than that. In one case the brain weight was 1,500 g., and the cranial capacity 1,690 c.c., a difference of 190. This was a case of a white male, suffering from manic-depressive insanity. Another case was one of senile dementia, in which the brain weight was 1,010 g., and the cranial capacity 1,360 c.c. The dura in the first case weighed 69 g., and in the second, only 40 g.

DR. J. H. LARKIN asked Dr. Rosanoff whether he had made any comparisons between putty and plaster-of-paris. He stated that some investigators had had very great success with plaster-of-paris impressions. There seemed also to be some difficulty in the pliability of putty in securing an impression of the cranial cavity, as putty was very variable and offered great difficulty in its application. The conclusion, he thought, seemed to be that plaster-of-paris which had been through a certain process whereby hardening did not readily take place, gave impressions which were more thorough and scientific. The application of the method advanced by Dr. Rosanoff, while not exactly new to him, offered some mechanical difficulties. Dr. Larkin's question, how-

ever, was merely on a point of information, as he had taken several measurements himself, but had given some of them up on account of the unreliability of putty, and now relied entirely upon the plaster-of-paris method.

Dr. Rosanoff, in reply to Dr. Larkin, said that for taking an impression of the cavity, plaster-of-paris would probably be very satisfactory. But his method was for the purpose of volumetric measurement only. Dr. Rosanoff said that plaster-of-paris, after becoming solid, and after immersion in water to ascertain the volume, would absorb enough water to render the method liable to considerable error. Moreover, the composition of putty was of no moment, as it was quite suitable for determining the volume of the cavity. The error that does creep in is within 1 per cent., this last being due apparently to the difficulty of fitting the skull cap over the base of the skull with sufficient accuracy.

STUDIES IN HEREDITY IN CANCER OF THE WHITE RAT.

I. LEVIN, M.D., AND M. J. SITTENFIELD, M.D.

It is hardly possible to come to a definite conclusion at present in regard to the influence which heredity exerts on the occurrence of human cancer. A study based on a statistical analysis of hospital cases seems to indicate that this influence is very small. But the material is most probably not well suited to this inquiry. More promising results ought to be expected from an analysis of the so-called "cancer families" in accordance with the modern methods of genetics. This method consists in collecting data not only of the members of the family suffering from cancer, but also of all the other normal members of the

same family. All the members are then divided into respective
generations of relationship to each other and then the numerical
difference is studied between the cancer cases in the different
generations of a "cancer family" and an apparently normal fam-
ily used as a control. This method will most probably enable us
to approach the solution of the question in human cancer. But
the work is just barely begun and it will require a great deal of
study before conclusions can be drawn.

It would seem *a priori* that it is a great deal easier to study
the subject experimentally on cancer of the white rats or mice.
The life cycle of these animals is only about two years and
during the decade of extensive research on the tumors of these
animals there were many opportunities to obtain several genera-
tions of the same stock. But thus far there has been little ac-
complished in the matter.

Bashford approached the subject experimentally in the fol-
lowing way: He removed surgically tumors occurring spontane-
ously in white mice, bred these mice with each other or with
the offspring of cancerous parents, and then studied the fre-
quency of the occurrence of cancer in the offspring. The work
has continued for several years, and it has not been possible to
detect any evidence that the liability to cancer has been enhanced
by systematic in-breeding. The difficulties in an analysis of the
results of this method of research are apparent and similar to
the difficulties that obtain in an analysis of simple statistical data
in regard to heredity—namely, the whole number of cases in the
offspring is so small that no correct comparison can be made with
the percentage of tumors occurring in stock animals of the
cancer age.

Tyzzer attacked the subject from a different standpoint.
He studied the influence of heredity in mice with reference to
their susceptibility to transplantable tumors. He found that a
certain tumor which originated in a Japanese waltzing mouse
was very readily transplantable in this variety of mice, but
could not be transplanted at all in a common albino mouse. He
then crossed the common albinos with Japanese waltzing mice

and inoculated the Japanese tumor into the offspring. His results showed that the hybrids of the first generation were then slightly more susceptible to the tumor than the Japanese waltzing mice, but the hybrids of the next generations, second as well as third, proved to be absolutely insusceptible to this tumor. Tyzzer concludes that the susceptibility of an animal to an inoculable tumor is neither inherited in accordance with Mendel's law, nor are the results obtained from cross breeding explained by any other known principle of inheritance.

While the study of inheritance in transplantable tumors of the mouse or rat offers less possibility for direct analogies with heredity in human cancer than studies on spontaneous cancer of the same animals, the ease with which experiments can be varied in transplantable tumors offers better promise for solving the question, and it seems to be clear from Tyzzer's results that there exists a certain kind of hereditary transmission in these tumors. But Tyzzer's method is too complex for a clear analysis in accordance with modern studies on genetics.

It may be well to present here in a few words the salient features of the science of genetics, as studies on heredity are called at present. The fundamental laws of the science were discovered by Gregor Mendel in 1865, but they passed unnoticed until they were re-discovered simultaneously by de Vries, Correns, and Tschermack in 1900. Mendel subjected to an experimental analysis the commonly known fact that an offspring may resemble in its different traits of character one or the other parent. He argued that a multicellular organism develops not from a single germ-cell or gamete, as it is called in genetics, but from a zygote, by which is meant the resultant of the union between the paternal and maternal gametes. Consequently, in order to learn the fate of parental characteristics in the offspring, certain simple features have to be selected in each parent and studied in the following generations. These simple features are called unit-characters, and in order to be able better to see the results of breeding, Mendel selected for his studies pairs of opposite unit-characters. For instance, in his studies on inheritance

in edible peas (*Pisum sativum*) he selected for one parent a tall
specimen and for the other a dwarf one. The cross-breed of
such a union is not a specimen of middle height, but all the off-
spring have the height of the tall parent. This fact of segrega-
tion of unit-characters represents the fundamental law in Men-
delian inheritance. By this is meant the phenomenon, that when
of two parents one possesses a certain unit-character, this
appears in one offspring and is absent in the other. The former
condition is called dominant and the latter recessive.

Thus of the offspring of two parents with opposite char-
acters, the first hybrid generation (F1), according to Mendelian
writings, all present apparently only the dominant character.
When this offspring is in-bred, there shows itself in the next
generation of hybrids (F2) a complete segregation of character;
not all the offspring possess the same dominant unit-character,
but only 75 per cent. show the dominant character and 25 per
cent. the recessive.

Now, if the entire F2 offspring should be divided into four
parts, of which three show the dominant character and one the
recessive, and then the different members should be inbred, the
results will show that the recessive quarter will always give only
a recessive offspring, or, as it is called in modern nomenclature,
will *breed true* to its character. One-third of the dominant off-
spring will also breed true to its dominance, while the remaining
two-thirds of the dominant, or consequently one half of the
entire F2 offspring, on in-breeding, will be *cross-bred* and will
result again in three-fourths dominant and one-fourth recessive.
These results indicate that a hybrid animal showing the recessive
unit-character will always breed true, while in the dominant hy-
brids some are true dominants and others contain both units.
The following table of Dr. Bateson's clearly illustrates this
scheme of Mendel's theory:

Parents   Tall (TT) x Short (tt)

F_1 Tall (Tt)

F_2

Tall	Tall	Tall	Short
TT	Tt	tT	tt
pure tall			pure short

F_3 TT   Tt   tT   tt   TT   Tt   tT   tt
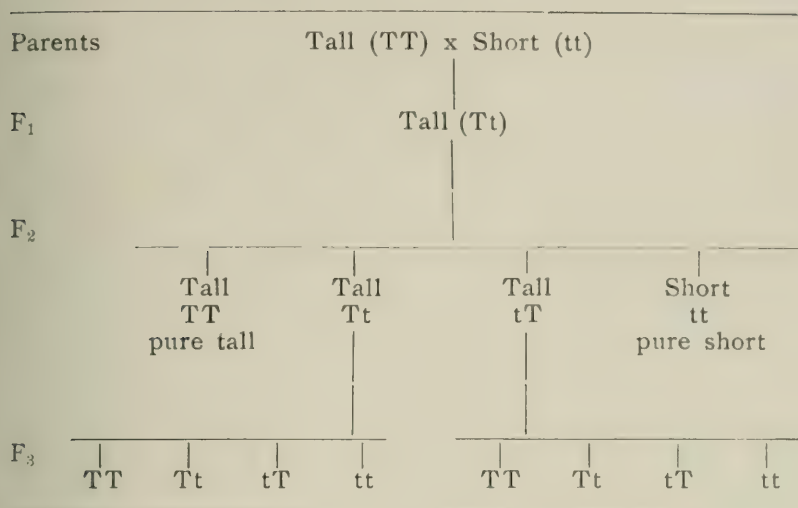
These so-called Mendelian laws of inheritance are easily demonstrated when one deals with simple characteristics like height, or color of flowers, etc.; but it must be understood that it is frequently extremely difficult to show clearly these Mendelian laws in breeding experiments, in view of the fact that each parent, and consequently so much more, the hybrid, possesses a great variety of unit-characters. It is furthermore shown that while certain characters segregate, in the Mendelian meaning of the term, others again blend and appear as a new character in the offspring. Even when one deals with a species which contains only a combination of segregating characters, the interaction between the latter may obscure results. The difficulties increase greatly when the investigation does not deal with simple unit-characters, but with the extremely complicated condition of the susceptibility of an animal to tumor growth.

It is well known that racial differences play an important role in the susceptibility of mice and rats to inoculable tumors, and it is natural to suppose that the hybrids of the waltzing mouse and common albino contain several unit characteristics exerting their influence on the susceptibility to the inoculated tumor. This is probably the reason why there was apparently no

regularity in Tyzzer's results. It is very interesting to note in this connection that he obtained different results in two sets of hybrids of the same first generation where the difference consisted in the fact that the common albino parents came from different stocks.

The first requirement for successful experimentation in genetics consists in selecting objects that will have as few opposite characteristics as possible. It seemed to the writers as the best plan of work to select as the only unit-characters to work with, the susceptibility or resistance of an animal to an inoculated tumor, but otherwise to in-breed within the same race. The work may be pursued in one of the following two ways: Either select tumor-bearing animals, remove surgically the tumors, and cross them; or else select animals that appear to be resistant to the inoculation. While both methods will be employed before final results are reached, it was to be expected that the offspring of immune animals would offer more striking results, since normally only a small percentage of the animals is resistant. Therefore the latter method was selected for the beginning of the work.

The results of the investigation obtained thus far, while not final, are so suggestive that it was considered advisable to offer them here. The experiments were done with Ehrlich's sarcoma of a white rat, a tumor of a very malignant type, which takes in from 80 per cent. to 100 per cent. of the animals.

Tumor resistant rats, or "Nullers," as Ehrlich calls them, were in-bred. Four litters were obtained of which the offspring lived long enough to be inoculated with the tumor. One litter of eight rats was born on the 15th of May, the second litter of six rats on the 19th of May, the third litter of seven rats on the 24th of May, and the fourth litter of two rats on the 2nd of June. On the 12th of August all the hybrid rats and twenty normal control rats, whose age and size were known and corresponded closely with the offspring of the Nullers, were inoculated with the tumor. The following table presents the result of the inoculation:

	Offspring of Nullers.	Controls.
No. of rats inoculated with tumor.......................... 23		20
No. of rats surviving at final examination................ 20		14
No. of rats with tumors 5		12
Per cent. of takes 25		86

The analysis of the table shows that while the tumor took in 86 per cent. of the control rats, it took in only 25 per cent. of the offspring of the Nullers. The result is very striking and tallies closely with Mendelian expectations.

The usual stock of white rats contains both resistant and non-resistant individuals, consequently a pair consisting of a resistant male and a resistant female would present, in Mendelian terminology, a first filial generation (F1) and the twenty rats bred from this first generation would represent the second generation (F2). Of these twenty rats fifteen were resistant and five non-resistant, showing a ratio of 3:1. Consequently, resistance to the growth of cancer in the white rat behaves like a dominant unit-character.

It is true that it is extremely difficult to interpret in accordance with the rules of genetics pathological conditions like a tumor growth, where the real pathogenesis is not yet clear. The objection may be urged, for instance, that the resistance was not transferred in this case through the gametes, but that certain antibodies circulating in the blood of the mother may have been transferred to the offspring through the placental circulation. In view of this, another set of experiments will be undertaken, where only the males are resistant. But even now it would seem to be difficult to explain on the assumption of placental transfer, that not all of the offspring became resistant, when both parents presented that characteristic, but only a certain percentage of the offspring, and that the percentage so closely coincides with the Mendelian expectations. Besides, this is not the only instance in which resistance to a disease seems to depend on the presence in the germ cell of a Mendelian unit. There exist certain kinds of wheat which are very susceptible to a disease known as wheat-

rust, which is due to an infection with a fungus. Other varieties of wheat are immune to the disease. Biffen demonstrated that when an immune strain is crossed with a susceptible one, the first filial generation consists of susceptible strains only, while in the next generation there appear susceptible and immune strains in the ratio of 3 : 1—showing that in this case the susceptibility is the dominant unit-character.

As was stated above, the work has just begun. Experiments are under way with tumor-bearing animals, with crosses between resistant and non-resistant, and also with in-breeding in the following generations. But the results obtained thus far seem to be extremely suggestive and it appears possible that work of such character may be of importance both in the further elucidation of the questions in heredity and in the pathogenesis of cancer.

THE CONDUCTING SYSTEM OF THE HEART: ITS NORMAL ANATOMY IN MAN AND CERTAIN OTHER MAMMALS.

A. E. COHN, M.D.

Dr. A. E. Cohn demonstrated lantern slides showing the path of the conduction system of a horse's, a cow's, a dog's, and a human heart. The histology of the nodes was likewise demonstrated.

1. Section through the right auricle of a dog's heart, showing the sinoauricular node.

2. Sinoauricular node, from a child's heart.

3. Section of the membranous septum, showing the auriculoventricular node. The structure of this node is practically identical with the structure of the sinoauricular node.

4. Section of a cat's heart, showing rather more plainly the way in which the bundle divides.

5. Section of a rat's heart, taken from above downward, showing the relation of the conducting system to the interventricular septum.

6. Section of the same human heart shown before, taken from just where the membranous septum ends.

Sections were also shown of the glycogen content in a sheep's conduction fibers (Nagayo) and of Purkinje cells from a beef heart.

Discussion:

DR. H. A. STEWART remarked that it was gratifying that Dr. Cohn had paid some attention to the nervous components of the bundle of His. The tendency, he said, in working on the anatomy of the bundle of His had been to disregard such a thing as a nerve; even Tawara himself made only a very cursory mention of the fibres in the auriculoventricular bundle. He added that those who have supported the old neurogenetic theory could now hold up their heads with some confidence. As Dr. Cohn had already mentioned, Dr. Wilson of Chicago had produced a luminous article on the nerves of the auriculoventricular bundle. Dr. Stewart had had the pleasure of seeing sections made by Dr. Wilson, who had been able to demonstrate very clearly the presence of ganglion cells in the auriculoventricular bundle, the fibers being of a very distinctive character, running in bundles between the muscle fibers and cells. So that here there was a clear demonstration, not only of the fibers, but also of ganglion cells of a very complex mechanism. Those who have upheld the myogenetic theory have said that it is the muscular part of the bundle which conducts impulses, because this muscular part is found very early in the embryo; that it remains unchanged throughout life, and is unaffected by atrophy or hypertrophy. But there is no known physiological experiment which has proved that the conduction between the auricle and the ventricle is by muscle. Dr. Cohn had already very forcibly pointed this out. The working out of the details of the nervous mechanism will finally establish, without doubt, the correctness of the view that the conduction is by nerves, instead of by muscle.

A CASE OF PULMONARY STENOSIS.

CHARLES NORRIS, M.D.

Dr. Charles Norris presented a case of pulmonary stenosis in a child of six years, which up to within four weeks of death, had been in apparently perfect health. There was no history of syphilis or other previous illness except measles. A month before its admission to Bellevue Hospital the child's mother observed that its face was swollen, and from then on it ceased to play. It was taken to the hospital, where it rapidly developed general subcutaneous edema and ascites, but no pleural effusion. There was marked cyanosis.

At the autopsy there was found a tremendous hydropericardium, the pericardial sac occupying the whole anterior portion of the chest. The heart as a whole was about normal in size, but there was an extreme hypertrophy of the right heart. The right auricle was markedly hypertrophied with closed foramen ovale. There was a slight tricuspid stenosis with fresh, very minute verrucae. The pulmonary cusps showed an extreme stenosis barely admitting a small probe. The valves were large and greatly thickened and there was an extreme hypertrophy of the right ventricle, so much so that the normal relation as to size between the ventricles was reversed. The septum bulged into the left ventricle but was in no place defective. There was a slight nodular sclerosis of the mitral valve. The ductus arteriosus was closed.

CALCIFICATION OF THE HEART MUSCLE FIBERS.

ALWIN M. PAPPENHEIMER, M.D.

A most unusual site for the abnormal deposition of calcium salts is the striated muscle of the heart. Rokitansky in the third edition of his text-book (1856) describes an instance of this lesion in the following words: "the muscle-fibers were transformed into rigid, brittle, refractile rods." Von Recklinghausen refers to the condition, as does Orth in his Lehrbuch; neither writer gives a detailed description. The modern text-books either ignore the lesion, or content themselves with the mere mention of its possible occurrence. Hart,[1] in a recent article, was able to collect but thirteen cases from the literature.

Besides the case here reported, we have seen sections from a case of Dr. Heinecke in Leipzig which showed an identical lesion; but in the routine examination of many hundreds of sections of heart muscle, we do not recall a similar finding.

The patient in our case was a male, twenty-one years of age. He was admitted to the service of Dr. Rogers at Bellevue Hospital in November, 1909, and operated upon for acute gangrenous appendicitis with peritonitis. Following the operation and continued drainage there was a general subsidence of all acute symptoms. On December 14th, however, the patient developed a fecal fistula; on the following day his temperature rose, and from this time until his death, eight months later, he showed symptoms of chronic sepsis, with chills, high remittent fever, continued leucocytosis, progressive anemia and emaciation. Three operations for supposed subphrenic abscess failed to disclose the true condition. The medical treatment consisted in the administration of colon vaccines and thyroid globulins.

At the necropsy, there was found suppurative pylephlebitis, with recent thrombosis of the portal vein; multiple large abscesses of the liver; abscesses of the right lung; a large hypernephroma of the right adrenal, which showed a diffuse suppurative infiltration; a recent fibrinous pericarditis; marked degeneration of the kidneys, and a fecal fistula at the site of the old operation, walled off by adhesions.

The heart muscle is described in the protocol as being "extremely pale, soft, yellowish-brown."

The lime deposits in the myocardium of the left ventricle were discovered in the course of the routine histological examination. We can say nothing, therefore, as to the distribution of the calcareous areas, only a small piece being available for study. In all the sections examined, there were found sharply circumscribed groups of fibers impregnated with lime salts—as many as a dozen foci in a section roughly 1.5 by 0.5 cm. in size. The staining reactions are typical of lime salts; an intense blue with Delafield's hematoxylin, black with Heidenhain's iron hematoxylin, and with 5 per cent silver nitrate after the method of von Kossa. Upon the addition of the acetic acid to an unstained section, there is no evolution of gas noted; carbonates, if present, cannot be demonstrated.

The calcification is sharply limited to the muscle fibers themselves, and even with the delicate silver nitrate method, no granules can be found in the interstitium. Either the deposit is in the form of coarse granules, which occasionally are arranged in transverse and longitudinal rows following the discs and primitive fibrils; or the entire fibre, together with its lateral anastomoses, is diffusely impregnated. The contours of the calcified fibers are somewhat irregular, and the calcareous fibers appear somewhat thicker than the normal fibers in the vicinity. On the cross section, one sees that the entire fiber is not always uniformly affected. The lime may be deposited first either in the center or near the surface or in the form of scattered granules. In fibers cut longitudinally, only a segment of the fiber may be impregnated, or the process may be complete in one portion and but slightly indicated in another.

A careful study with Mallory's phosphotungstic and Heidenhain's iron hematoxylin stains has convinced us that the deposits of lime take place only in fibers which are the seat of advanced degenerative changes or complete necrosis. These necrobiotic changes are indicated by a loss of the transverse and longitudinal striations; by a pycnosis or complete disappearance of the nuclei;

and by disintegration of the muscle substance into a structureless
granular mass.   Only the general contour of the fiber is pre-
served.

These areas of focal necrosis—for such they are—are sur-
rounded by normal muscle fibers with excellently preserved
striations and normal nuclei.   Aside from the lesions described,
the myocardium is normal in all respects.
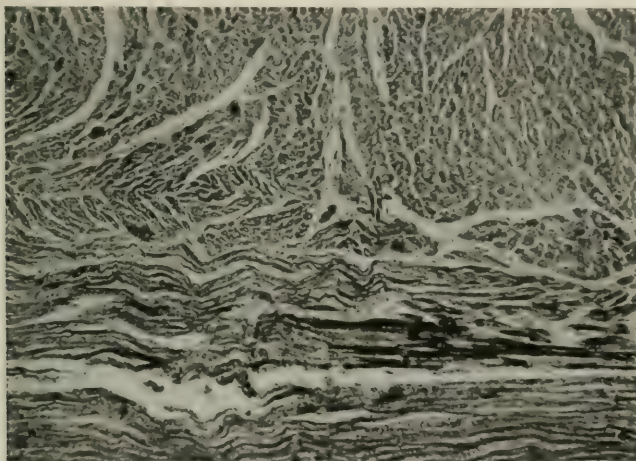
Calcification of the Heart Muscle Fibers.

A point of importance is the absence of all inflammatory
changes either in the areas of calcification themselves or else-
where.   In places there appears to be a slight proliferation of the
nuclei of the perimysium about the calcareous fibers, and there
may be found an occasional round cell.   Of a true myocarditis,
there is not a suggestion, and the lesion is distinctly not upon an
inflammatory basis.

Whether there is a relation between the deposition of lime
and a previous infiltration of fat, could not be determined in this
case because the material was preserved in alcohol.   There is
however, no marked vacuolation of the fibers in the necrotic
areas, nor did the appearance of the muscle in the gross suggest
advanced fatty change.   That there is no constant relationship

between fatty degeneration of the heart muscle and calcification, is evident. The former is a most common, the latter amongst the rarest of findings. Hart has given consideration to this question. In his case, no fat could be demonstrated with Sudan in the calcareous fibers, although in the periphery of the necrotic areas, he found fibers showing considerable fatty change.

With potassium ferrocyanide and HCl, a few of the calcareous fibers take an intense blue color; the majority show only a diffuse bluish tinge. This finding is of interest in connection with the much debated question as to the relation between iron and calcification in the tissues. Hart[1] in his case, obtained a positive iron reaction in the calcified fibers, but ascribes no importance to his finding. Sumita[2] in his thorough work upon the relation of iron to calcification, also states that he obtained a positive reaction in calcified heart muscle. He gives no further details of his case, but his observation is important because he worked with iron-free reagents and took every precaution to avoid artefacts. The presence of iron in these cases is of interest since it is evidently not hematogenous in origin.

Of the histological changes in the other organs, we shall refer only to the deposits of lime found in the liver, adrenal tumor, lungs and kidney. In the liver, the lime was found in the form of granular masses in the walls of the abscesses. In the hypernephroma of the right adrenal, the tumor tissue was largely necrotic and infiltrated with pus. Here, as in the liver abscesses, lime was present in the suppurative foci. In the lungs, the lime was present in the form of globular or cylindrical masses of considerable size. These were situated either in the veins themselves—(old thrombi?)—or in the perivascular lymphatics. There was no calcification of the capillary walls or of the elastic fibers. In the kidney, several irregularly globular deposits of lime were found lying in the cysts beneath the capsule. There were also a few foci deeper in the cortex; in one place, the lime forms a cast lying within a Henle tubule. Most of the deposits are distinctly in the interstitial tissue.

In reviewing the reported cases of calcification of the heart

muscle, we find that all authors agree that the deposition of lime is limited to the muscle fibers themselves, and to those only which show advanced degeneration. Fatty changes have been noted in the adjacent fibers (Roth,[3] Hedinger,[4] Wiechert,[5] Hart[1]), but not in those showing calcareous deposits. The collections of mono- and polynuclear cells which have been described about the calcareous areas, have been interpreted by a few writers as a primary myocarditis; more probably they represent a purely reactive inflammation about a calcareous foreign body, the lesion which precedes the deposition of the lime salts is a toxic necrosis of the muscle fibers.

The cause of the necrosis varies in the different cases. Hart's case was one of severe tertiary syphilis; Wiechert's, a case of paratyphoid A infection; Roth's a case of phlegmonous inflammation; in Askanazy's[6] case, there was an ulcerative endocarditis. Langerhans'[7] observation of a case of calcification of the heart muscle in association with chronic plumbism, shows that inorganic poisons may play a role. In our own case, the long continued suppurative pylephlebitis is the obvious cause for the toxic degeneration of the fibers.

We do not wish to discuss at length the broader problems concerned in the abnormal deposition of lime salts in the tissues. It is well known, since Virchow advanced his theory of calcium metastasis, that many cases of generalized deposits of lime in the different organs have been associated with destructive bone lesions—malignant growths, suppurative processes, and so forth. A typical case of this category is that recently reported by Tschistowitz and Kolessnikoff,[8] of multiple myeloma with extensive calcific deposits in the capillaries and elastic tissues of the lungs, in the glomeruli and membranae propriae of the kidneys, in the gastric mucosa, and in the media of various arteries. A similar case showing remarkable calcification of the endocardium of the left auricle, of the lungs and of the pulmonary veins, in a patient with myelogenous leukemia, has recently been reported by Verse[9] before the German Pathological Society. In cases of this sort the extensive halisteresis of the bones must be regarded

as at least a contributory factor in the process. On the other
hand, similar cases have been reported in which no destructive
lesions of the bones could be demonstrated, and to which the idea
of a "calcium metastasis" in Virchow's sense, does not apply.
The experiments of Von Kossa[10] and of Rüdel[11] have shown that
repeated injections of soluble calcium salts do not lead to calcifi-
cation of the tissues.

On the other hand, there are many familiar examples of
calcification associated with local necrosis of tissue, in which
there is nothing pointing to an increased calcium content of the
circulating blood, or to a failure in elimination. The calcareous
incrustation of necrotic ganglion cells in the brain of general
paresis is an illustration of calcification due to a purely local
condition.

In the case here presented, there was no destructive bone
lesion evident, although a complete examination of the bones
could not be made. Furthermore, there is no reason to suppose
on histological grounds that there was a failure on the part of
the kidney or intestine to eliminate calcium properly, although
only a chemical study of the excretions during life could have
given us positive evidence of such an insufficiency.

All that we can say as regards the calcification of the heart
muscle in this case is that it appears to be conditioned by a local
necrosis of the muscle fibers; and for this local necrosis, we have
sufficient cause in the long standing pylephlebitis. The necrosis
is apparently of toxic origin and not due to infarction or to
local myocarditis. The underlying cause for the calcific deposits
in the lungs and kidney is less clear but in all probability they too
are associated with similar local lesions of toxic origin. The lime
deposit in the exudate of the chronic liver abscesses, needs no
special comment.

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A CASE OF TUMOR OF THE PANCREAS.

RUSSELL L. CECIL, M.D.

Dr. Cecil presented a case of a tumor occurring in the pancreas of a male, aged 63, who came to autopsy at the Presbyterian Hospital on November 3, 1908. The anatomical diagnosis was adenocarcinoma of the ascending colon and chronic interstitial nephritis. The tumor of the pancreas was discovered quite by accident. Microscopically, the tumor was about the size of a pea, and was located near the surface of the pancreas. It was surrounded by a very narrow zone of pancreatic tissue, from which it was sharply defined.

Microscopically, the tumor was composed of masses of cells separated by a framework of connective tissue, which in many places was hyaline. The tumor cells were small, of a polyhedral shape, arranged in irregular cords. In some places the hyaline degeneration had involved the tumor cells. The supporting framework contained capillaries. The tumor was separated from the surrounding pancreatic tissue by a thin fibrous capsule.

Dr. Cecil said that the question arose whether the tumor originated from a duct, an acinus, or an island of Langerhans. From the appearance and arrangement of the cells he concluded that the tumor was an adenoma originating from an island of Langerhans. It was interesting to note that the islands of this pancreas showed the peculiar adenomatous hypertrophy, described by Reitmann, MacCallum, and others, which has generally been found in association with diabetes. There was, however, no record of a glycosuria in Dr. Cecil's case.

Discussion:

Dr. W. G. MacCallum said that some time ago he had seen a case of almost exactly similar character described in some detail by Dr. Helmholz in the *Bulletin of the Johns Hopkins Hospital*. In that case, as in this, the nodule was regarded as an adenoma arising in the island of Langerhans, and it was thought that possibly it might act in some compensatory way for other

islands of Langerhans. It had interested him especially, there-
fore, to hear what Dr. Cecil had had to say about the other
islands of Langerhans in this particular pancreas. In another
case in which there was diabetes the islands of Langerhans
seemed more or less atrophied; but there were other islands,
thought to be secondarily developed, to compensate for those
which had atrophied.

DR. CECIL, in closing the discussion, said that in addition
to Dr. MacCallum's, Dr. Nicoll's case (the photographs of which
showed the tumor to be almost identical with his) was the only
other case he had seen reported.

A PRELIMINARY REPORT OF EIGHT CASES OF ADAMANTINOMA.

ELISE L'ESPERANCE, M.D.

The frequency of occurrence, the peculiarities in the histo-
logical structure, the difficulties in diagnosis, and the specific
origin of various tumors of the jaw, now generally called ada-
mantinomas, seem to demand greater attention than is commonly
accorded them.

A brief résumé of our knowledge of these tumors may be
permitted, preliminary to outlining the histological structure of
several tumors of this class that have been studied in the Path-
ological Laboratory of Cornell University.

This interesting group of neoplasms was described by
Magitot, one of the earliest observers (1875), as a cystoma or
multilocular cyst of the jaw. The tumors were believed to have
their origin from the surplus or retarded development of the teeth,
this view being accepted by him as well as by Falkson, Eve, Bayer,
and others of this period. Later Büchtmann (1881) assumed
that they arise from the buccal mucous membrane, or the buccal

mucous glands. The fact that they are derived from remnants of the enamel organ was first recognized by Malassez in 1885, and verified later by Kruse, Chibret, and others. On account of this origin they have frequently been called adenoma adamantinum.

The enamel organ is formed by an infolding of the ectodermal layer which caps the dental papilla. It is composed of a superficial layer of polyhedral cells, with an inner layer of high columnar epithelium, the adamantoblasts, between which lies a layer of highly peculiar reticular or stellate cells, the stratum mucosum.

The true adamantinoma, therefore, should show some features of these structures. Kruse based his conclusions on the fact that in his three cases he observed this typical structure of the enamel organ. Chibret's case also contained these types of epithelium.

Adamantinomas occur as cysts or solid new growths, either in the upper or lower jaw; according to some authors between the ages of six and twenty-five years, that is, at the time of the eruption of the teeth. But Massin has reported a case in a newborn infant, and Chibret one in a patient fifty-three years old. Our cases all developed in middle life, bearing no relation to the eruption of the teeth.

A considerable number of these tumors assume the form of simple or multilocular cysts, the so-called dentigerous cysts, excavating the alveolar process. Into these cysts papillary outgrowths occasionally develop and partially developed teeth have been found within them.

Adamantinomas are not malignant in that they do not form metastases (with the exception of one doubtful case reported by Eve in which he observed metastases in the lumbar lymph nodes and the suprarenals) but they infiltrate extensively the bony envelope, with atrophy of the osseous structure, sometimes splitting the bone.

They show, however, a strong tendency to recur locally, which was noted in several of our cases.

We have made a more or less arbitrary classification of these neoplasms, according to the type and arrangement of their epithelial cells, into three groups:

1. Acanthomatoid.
2. Plexiform.
3. Glandular.
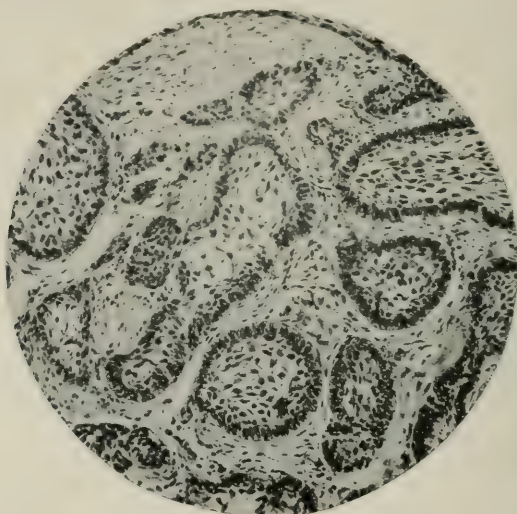
Figure I.

Between these types all degrees of variation exist. *The first group* shows the simple epithelioma composed of stratified squamous epithelium, in which many of the cells have undergone degeneration, in which condition they closely resemble the central cells of the enamel organ. The cellular elements are irregular, both in character and arrangement, many showing areas of horn-ification. In one specimen a single mass shows clear cells in one portion, undergoing hydropic degeneration, and in another contiguous area, typical hornified cells. I use the term hornified tentatively, as Borst has shown that endothelial cells undergo a hyaline degeneration, very closely resembling true hornification, which can be positively identified only by demonstrating the presence of striations, spines at the borders of the cells and kerato-hyalin granules. As I have not been able at the present time to show these characteristic features, I leave this for later study.

Figure II.

The second class comprises a type of tumor, in which the main portion is embryonal in character, and is composed of a fibrillar connective tissue stroma in which ramify convoluted masses of irregular epithelial cells.

These masses vary both in size and distribution, but as a rule closely resemble embryonal epithelium. Occasionally one observes areas that are composed of stratified squamous cells, developing pearls in the midst of this plexiform arrangement.
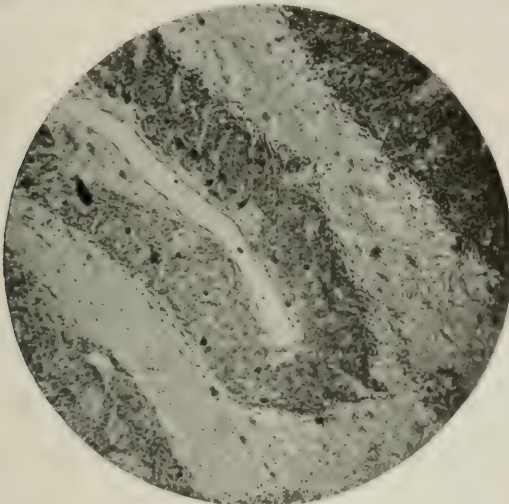

Figure III.

The third class is made up of large columnar epithelial cells arranged in rows or alveoli, producing a glandular structure. On cross section these rows appear to have a lumen, from the manner in which the cells surround the blood vessels. The existence of true lumina is doubtful. This type is apt to be vascular and show areas of hemorrhagic infarction.
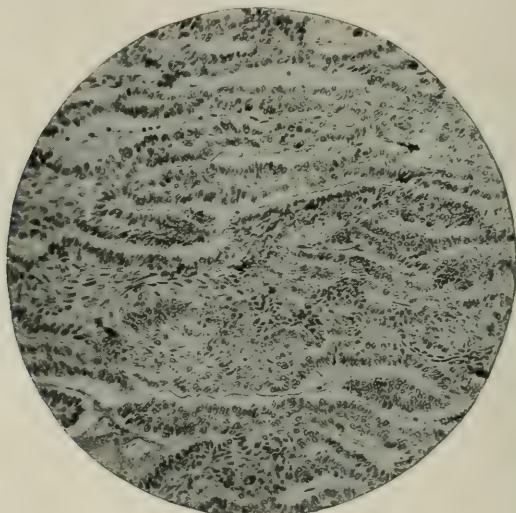
Figure IV.

In few other neoplasms does one see a more remarkable degree of metaplasia, than has been observed in the epithelial cells of a recurrent adamantinoma of this type, in which all variations were seen from the squamous epithelium of the simple epithelioma to spindle-shaped cells closely resembling spindle cell sarcoma, later assuming a diffuse round cell character, so similar to a round cell sarcoma that one would be in doubt concerning its true character without a knowledge of the clinical history and the previous specimens.

It is necessary therefore to differentiate adamantinomas not only from basal cell epitheliomas, for which they are sometimes mistaken, but also from spindle and round cell sarcomas, and a positive diagnosis, in some cases can be made only after careful study of the histological structure and clinical history.

Case I.—Acanthomatoid in type showing many resemblances to a simple epithelioma.

This tumor was scraped out of the tooth socket.

Case II.—Adamantinoma of the acanthomatoid type with groups of cells surrounding high columnar adamantoblasts.

Case III.—Adamantinoma resembling a simple epithelioma with high columnar cells, markedly reticular in center with one area showing cysts. A single mass in this tumor shows clear cells in one portion undergoing hydropic degeneration and an area of hornified cells.

Case IV.—Plexiform adamantinoma of the left ramus of the lower jaw. The clinical history is briefly:

Mr. M——, age thirty-seven years, admitted to St. Francis Hospital, November, 1910, in the service of Dr. Rogers, to whom I am indebted for the clinical history and material. The tumor was first noticed one year ago, growing slowly, to within the past month, when it began to increase very rapidly. The skin was adherent and of a bluish color over the site of the tumor, which appeared quite vascular, but not ulcerated. Microscopically the specimen shows the typical plexiform structure, masses of epithelial cells infiltrating the connective tissue. Many of these masses of epithelial cells show degenerated and necrotic areas. The outer layer shows columnar epithelium, gradually becoming cuboidal until the cell outline is lost as they reach the necrotic portion.

Case V.—Glandular adamantinoma with plexiform arrangement. Shows many glandular characteristics. High columnar cells, enameloblasts and areas of hornified cells.

Case VI.—Glandular adamantinoma, marked glandular arrangement with peripheral layer of enameloblasts and spindle reticular cells in the center. Tumor recurred two years later, showing practically the same structure.

Clinical history: Mr. L——, age thirty-nine years, first noticed slight swelling of the gum and occasional bleeding after

extraction of the first upper molar tooth in 1906. A few months later a small mass of tissue protruded from the tooth socket and was removed by a curette. About a year later, November, 1908, there was moderate thickening of the alveolar border and more bleeding tissue protruded from the socket. Section of a portion of this tissue showed the structure of a glandular adamantinoma. Partial resection of the superior maxilla revealed that the tumor had filled the antrum. On April, 1909, the tumor reappeared in the scar. Complete resection of the maxilla and pterygoid process of the sphenoid was attempted, but the patient died a few hours after the operation. The tumor had invaded the masseter muscle, the floor of the orbit, and the posterior wall of the pharynx. There was no involvement of the lymph nodes.

Case VII.—Glandular adamantinoma showing glandular arrangement with a typical layer of enameloblasts.

The next case is the most interesting of the series, and I shall give it in some detail.

Case VIII.—A recurring adamantinoma appearing as a plexiform epithelioma, recurring as a large alveolar and spindle cell tumor, and eventually as a round cell perithelioma.

Clinical history: Mrs. X——, forty-six years of age. In November, 1906, the removal of a molar tooth was followed by some inflammation of the maxilla, with a discharge of pus.

This was succeeded by a slight permanent swelling of the alveolar border. For one year there was slow enlargement of the gum. In December, 1907, there was frequent slight epistaxis. In May, 1908, a small tumor mass was found protruding into the inferior nasal passage, a portion of which on section was found to show the structure of a plexiform epithelioma. Resection of the superior maxilla was performed. The entire horizontal ramus of the jaw bone was much thickened, and the seat of a plexiform epithelioma which had eroded the dense portions of the bone and extended into the antrum. There was no involvement of the skin nor of the buccal mucosa.

In October, 1908, a recurrent nodule as large as a marble

presenting on the mucous surface of the superior nares was removed and found to have the structure of a large alveolar and spindle cell sarcoma. A second nodule beneath the skin at the upper border of the malar bone was removed November, 1909. It had the structure of a large round cell perithelioma. A third recurrence in the same region, August, 1910, had the structure of a perithelioma or a diffuse round cell growth.

Discussion:

Dr. James Ewing stated that he and his associates had been very much impressed with the frequency of occurrence and variety of structure of the tumors presented by Dr. L'Esperance, and on that account had thought it might interest others to see some of the specimens which had aroused this interest. Not only did these tumors occur with greater frequency than one might imagine, but they offered some very interesting observations on certain tumor processes. Especially in this last case the type of metaplasia had puzzled them a good deal. As a matter of fact, this tumor had been followed by them in New York and also by eminent pathologists in Boston, and some added interest was lent by a difference of opinion which had arisen as to the significance of the later tumors found in five operations. They were all agreed that the first two tumors were epitheliomas. As to the first specimen, however, they were not in accord as to its adamantinoma origin. When the third specimen arrived it was found to be composed of very small and indifferent cells. Dr. Mallory being out of town, another Boston pathologist pronounced it a spindle cell sarcoma. The fourth specimen caused much wonder as to whether they were really dealing with a tumor which had started with squamous cell epithelioma. Dr. Ewing felt compelled to maintain the position that the tumor had throughout been an epithelioma. The fifth specimen showed a diffuse round cell growth, which had no resemblance to any common form of epithelioma. They had to do here, he thought, with a degree of metaplasia which is extremely unusual, and an ac-

quaintance with which is necessary if one is to be a safe diag-
nostician in this particular field.

DR. E. MOSCHCOWITZ referred to a congenital epulis which
he had studied a few months ago. The tumor at birth projected
from the mouth, was the size of a walnut, and was attached by
a pedicle to the incisor teeth. Microscopically, the tumor pre-
sented a picture totally different from any other that he had ever
seen. It was composed of large polyhedral or elliptical cells be-
tween which were delicate bands of connective tissue. In one
portion of the tumor there were epithelial inclusions. After care-
ful study, Dr. Moschcowitz had come to the conclusion that the
tumor had its origin in the papilla, and, more particularly, in the
odontoblastic layer of the developing tooth, and that the epithelial
structures were remains of the enamel organ. He had applied
the term "odontoblastoma" to this tumor. The tumor was in-
teresting in connection with those described by Dr. L'Esperance,
inasmuch as it represented a growth from the connective tissue
elements of the developing tooth, as opposed to the adamantino-
mas in which the epithelial origin is predominant. Dr. Mosch-
cowitz thought that the case of Massin which Dr. L'Esperance
had quoted as a congenital adamantinoma was a tumor similar
in structure to his own. It was interesting to note that all the
"odontoblastomas" thus far reported were congenital.

DR. I. LEVIN asked whether there might not be a possibility
that in these tumors one might find cells of varying natures in
different parts of the specimen. He sought to explain the ap-
parent change by saying that when a great number of sections
of the same tissue are examined there might be enough variation
in the cells of the different parts of the same growth to mislead
one into the belief that they were sections of another tumor. He
disagreed with the explanation given by Dr. Ewing, i. e., that
there was a kind of metaplasia; and offered his as being the better
explanation of the apparent change in the character of the tumor.

DR. A. O. J. KELLY expressed himself as being entirely in
accord with Dr. Ewing's views. He had seen many cases in the
German Hospital, Philadelphia, which were similar to the one

under discussion. Often, in his experience, he had found several
records of the same specimen presenting conflicting diagnoses.
On the whole, he felt quite confident that this was not to be
attributed merely to an apparent change resulting from examin-
ations of various sections of the same tumor (which was the
theory advanced by Dr. Levin) ; but thought that the metaplasia
must have occurred in a recurring growth of the tumor. Dr.
Kelly had seen many cases which revealed many histological
features, which one would never recognize, at first sight, as
recurrences of a former tumor. He said, in addition, that the
metaplasia found in recurring tumors of this kind was very
extraordinary indeed.

# ACUTE LYMPHATIC TUBERCULOSIS WITH
PURPURA HEMORRHAGICA.

W. B. COLEY, M.D., AND JAMES EWING, M.D.

Mrs. P——, aged forty-two, married, four children, no
family history of tuberculosis, no history of syphilis or cancer.
Had always enjoyed vigorous health up to onset of present ill-
ness. About November 20, 1909, she noticed enlargement of
cervical lymph nodes on both sides, principally posteriorly to the
right sternomastoid muscle. The swollen nodes gradually in-
creased in number and slowly in size, accompanied by some fever,
anorexia, weakness, and loss of flesh. Early in December she
had sore throat of moderate severity. Her husband states that
there was some sore throat preliminary to the swelling of the
cervical nodes. In December there were recurrent attacks of
nausea and vomiting. About December 5 a hemorrhagic erup-
tion appeared chiefly over the face, consisting of pin-point and
broader superficial petechiæ most marked below the eyes. The
eruption increased with the attacks of vomiting.

On admission to the hospital, in the service of Dr. Coley, she was weak but able to walk; T. 101-102° F., pulse, 118. The nodes on both sides of the neck, chiefly behind the sternomastoid muscle, were enlarged to the size of a bean or hickory nut, and several were found in front, but none in the axillae or groins. There was a marked hemorrhagic eruption on the face, and extending to neck, arms, and body were numerous minute petechiae. The spleen was slightly enlarged. There was no pain except from sore throat.

Blood examination (Ewing), December 13: Red cells, 2,480,000; hemoglobin, 70 per cent.; leucocytes, 5,500; mononuclears, 88 per cent.; polynuclears, 12 per cent.; eosinophiles, none. Culture on ordinary media negative. December 19: Red cells, 2,288,000; hemoglobin, 55 per cent.; leucocytes, 8,000; large non-granular mononuclears, 21 per cent; medium sized basophilic mononuclears, 63 per cent.; polynuclears, 16 per cent. Urine, highly colored, specific gravity 1,024, a trace of albumin, a few hyaline and granular casts, no sugar, heavy indican reaction. Culture from throat on blood serum yielded streptoccocci but no Klebs-Loeffler bacilli. A cervical lymph node above the clavicle was removed for histological examination. On December 13 the patient was seen in consultation with Dr. L. A. Conner, and the conclusion reached that the disease might be acute leukemia without leucocytosis, or acute Hodgkin's disease. Section of the lymph node later gave none of the specific signs of Hodgkin's granuloma, but showed the structure of a diffuse lymphoma or excessive inflammatory hyperplasia of large mononuclear cells with numerous mitoses. The sinuses, follicles, and cords were obliterated, and it was impossible to distinguish the lesion from a leukemic process.

The condition of the patient grew rapidly worse, the temperature rose to 104-106° F., by December 17, and remained at that level without definite remission. The vomiting recurred. The eruption became diffuse and innumerable fine and large petechiae appeared over limbs and body. The arms were completely covered by successive crops of petechiae, at first brilliant
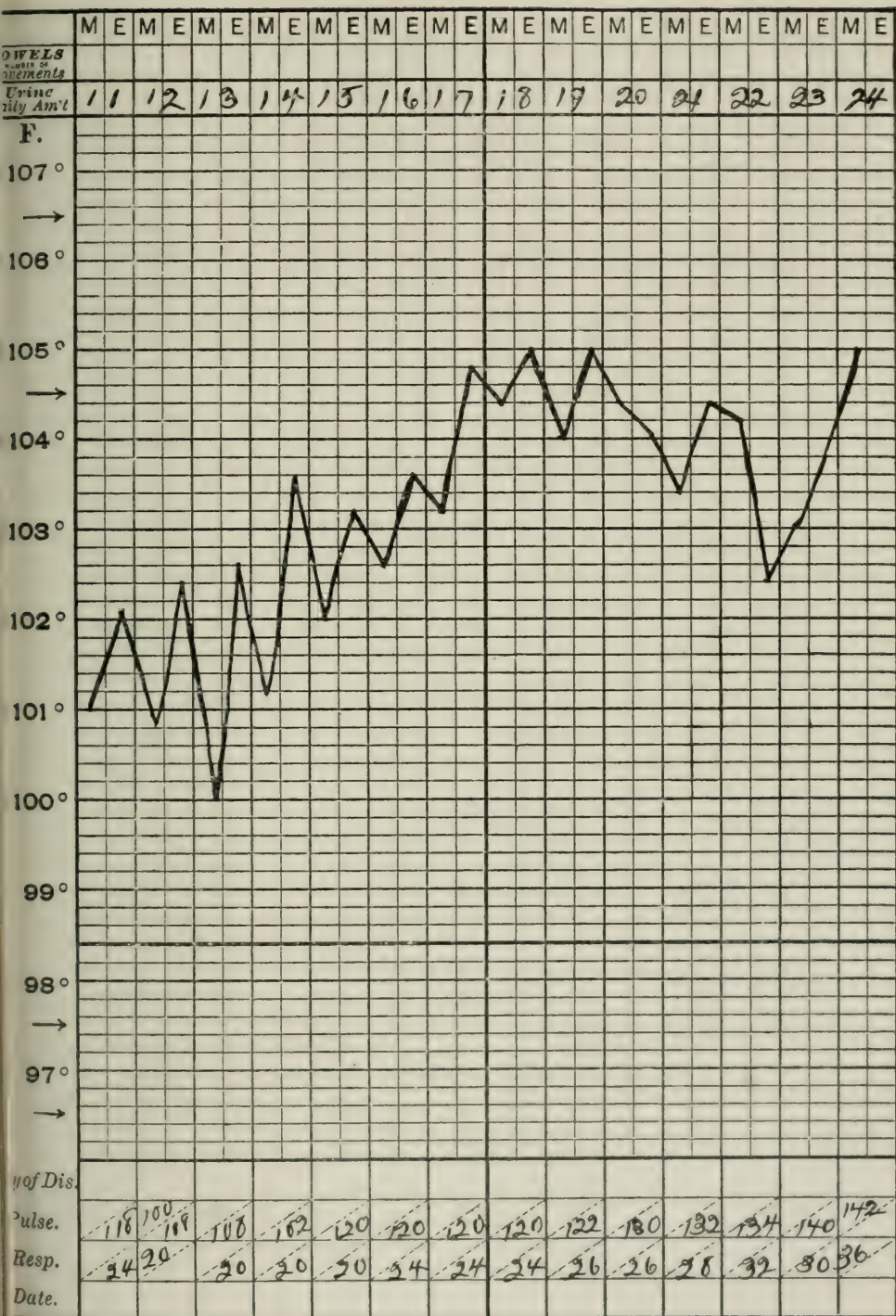
red, later becoming brownish. December 19 blood culture was again negative. There were no hemorrhages from the mucous membranes. The patient passed into a state of semi-coma, which persisted for several days until her death, December 24, at 12.30 p. m.

Report of post-mortem examination, December 24, 1909, four hours after death, by Dr. Ewing:

Body of a large, well-nourished woman. No rigor; no edema. There is a profuse, universal hemorrhagic eruption of the skin, consisting of minute points becoming confluent, forming flat petechiae in many places, especially on arms, and diffuse all over face. Some points are recent and bright red, others of longer duration and slightly brownish. The buccal mucosa shows a few medium sized petechiae. Lymph nodes of neck are moderately enlarged, firm; those in axillae and groins slightly enlarged.

Heart, normal; right chamber filled with dark fluid blood.

Lungs—There is a partial consolidation of posterior portions of both lungs. Section is very deep red, intensely congested, and shows minute hemorrhages and areas of consolidation as of lobar pneumonia. Bronchi intensely congested; no signs of tuberculosis.

Pleura shows a thin layer of fresh fibrin and many petechiae.

Liver—Size and consistence normal. Surface shows a few subserous hemorrhages. Surface and section show many whitish foci, miliary to the size of a pea, as of irregular tubercles. Parenchyma deeply congested, markings obscure.

Spleen—Moderately enlarged, 14 x 8 x 5 cm., firm, pulp grayish red, follicles visible as minute gray points.

Pancreas—Normal.

Peritoneum—Shiny, normal, except for a few small petechiae.

Stomach—Mucosa distinctly thickened, the folds being unusually high; but no enlarged follicles are visible. It shows some small hemorrhages. Small intestine not examined.

Colon—Shows uniform swelling of all solitary follicles, a very few of which show superficial erosions.

Pelvic Organs—Normal.

Kidneys—Capsules are mottled with many small hemorrhages. Section shows cloudy swelling with intense congestion of medulla.

Lymph Nodes—The bronchial, thoracic, retroperitoneal, and mesenteric lymph nodes are enlarged, soft, intensely congested, with small hemorrhages, and show many miliary to pea-sized grayish areas resembling tubercles. The largest nodes are the thoracic, which measure 1-3 cm. in length. They are softer and more acutely inflamed than ordinary tuberculous lymph nodes.

Anatomical Diagnosis—Subacute granuloma of lymph nodes, probably tuberculous; tuberculosis of liver; acute exudative pneumonia. Miliary and diffuse hemorrhages of skin, serous membranes, and renal capsules. Diffuse hyperplasia of lymphatic system of stomach, colon, cervical, thoracic, abdominal and axillary nodes; pharyngitis.

Microscopical Examination—Lymph node of neck removed at operation. Section shows diffuse hyperplasia of large mononuclear cells with vesicular nuclei, obliteration of sinuses, cords and follicles. There are no tubercles or necrosis. There are some mononuclear giant-cells. There are many mitoses. Thoracic and abdominal lymph nodes show intense congestion. The tubercles show liquefaction rather than caseous necrosis. They are surrounded by very many phagocytic cells containing ten to fifty englobed leucocytes. The nodes show diffuse hyperplasia of mononuclear cells similar to that described above. Stains for tubercle bacilli revealed a very few elongated strongly acid-fast bacilli resembling tubercle bacilli; they were found only in the necrotic foci.

Liver—There is general granular degeneration of the liver cells with intense congestion. The portal canals are infiltrated with a thick mantle of large mononuclear cells. The tubercles visible in the gross include the portal canals and a few show

liquefaction necrosis. Here a few strongly acid and alcohol-fast bacilli are found resembling tubercle bacilli.

Spleen—There is diffuse hyperplasia of large mononuclear cells obliterating cords and sinuses and encroaching upon the follicles.

Kidneys—There is diffuse granular degeneration of the tubule cells. Many miliary lymphomata are scattered throughout the cortex and medulla.

Stomach and Colon—In the mucosa there is marked hyperplasia of solitary follicles, many of which are the seat of superficial ulcers.

The bone marrow in the vertebral bodies is intensely congested and the sinuses are gorged or ruptured. There is a feeble hyperplasia of large mononuclear cells. Islands of nucleated red cells are missing, and the marrow cords are obliterated.

Diagnosis—Subacute lymphadenitis and hepatitis due to infection by tubercle or tubercle-like organisms. Hyperplasia of lymphatic system. Miliary lymphomata of kidney. Exudative pneumonia.

Bacteriological Study—By Dr. Ewing and Dr. Frank M. Huntoon.

Cultures of retroperitoneal lymph node on glycerin egg medium, made December 24, gave a slight growth of an acid-fast bacillus resembling the tubercle bacillus, first seen on February 11. All other cultures negative. Of five monkeys inoculated intravenously on December 28 with emulsion of lymph nodes, three died in a few days of gastroenteritis, one of general tuberculosis on February 3.

The fifth monkey died on April 11, of general tuberculosis, most marked in the omentum and liver, with oldest lesions in the inguinal lymph nodes at the point of inoculation. A sixth monkey inoculated with 5 c.c. of blood serum drawn December 19, died March 24 of general tuberculosis very abundant in the lungs, liver and spleen. Five guinea pigs and four rabbits were inoculated with lymph node emulsion intraperitoneally or intra-

venously. One guinea pig, inoculated December 28, died February 28 from tuberculosis of mesenteric vessels due to a single large granulomatous mass in mesentery. No tubercle bacilli were found in this mass and cultures were negative. The mass consisted of inflamed lymph nodes, showing lymphoid hyperplasia, edema, but no necrosis. Of two guinea pigs inoculated on January 25 with 2.5 c.c. emulsion of liver which had been kept on ice, one died on March 6, of general tuberculosis. From the spleen a pure culture of tubercle was obtained.

Four rabbits were inoculated intravenously with 0.5 c.c. of emulsion of lymph node. They failed to show any external sign of disease at the end of six months.

The foregoing case presents several remarkable features, and in some respects is unique. Tuberculosis running an acute course of six weeks, with continuous fever, universal hemorrhagic eruption, systematic involvement of lymphatic organs, bacteremia, and absence of specific lesions in the lungs, is a clinical type of the disease not described in current text-books of medicine, and so far as we can learn not previously observed.

The most notable feature of the case is the limitation of the disease chiefly to the lymphatic system, that tissue which ordinarily possesses a relative immunity to this infection. The earliest lesions were those of the cervical lymph nodes from which the infection spread through the mediastinal and abdominal nodes, eventually producing multiple miliary lesions of the liver and spleen. In addition to the focal lesions in which tubercle bacilli were abundant, there was a diffuse hyperplasia of the lymphatic structures of the stomach and intestinal tract. The bone marrow showed a draining of leucocytes with occasional focal hyperplasia. In the liver there was extensive lymphoid infiltration of the portal canals without demonstrable bacilli, and numerous larger necrotic lesions in which bacilli were present.

The histological structure of the necrotic lesions containing bacilli was peculiar. These lesions were of acute exudative and hemorrhagic character ending in central necrosis. They contained giant macrophages inclosing twenty to fifty lymphocytes,

and were quite different from any cells seen in ordinary tuberculosis. In the lymphomatous areas not containing bacilli, in the cervical node removed during life, in the portal canals, and in the wall of the stomach and colon, the lesions were indistinguishable from those found in many cases of lymphatic leukemia. The pneumonia was a terminal process which the clinical signs indicated as of a few days duration. It was, however, at least partly of tuberculous nature, streptococci being abundant and tubercle bacilli being present in small numbers in a few areas of necrotic bronchitis.

The blood picture suggested the diagnosis of acute leukemia. There was marked relative and slight absolute lymphocytosis. Many of the lymphocytes were of very large size with large nuclei. In the smaller cells azure granules were abundant. Blood examinations have been reported in several cases of tuberculous purpura, all of which showed little or no leucocytosis but excess of polynuclear cells. The striking relative lymphocytosis of the present case is therefore an exception to the rule. The suspicion of leukemia was strengthened by the structure of the cervical node removed on December 13, which could not be distinguished from a leukemic process. The anemia and the hemorrhagic eruption also encouraged the belief in the leukemic nature of the disease, and it was this belief that led to the inoculation of several monkeys. The association of tuberculosis with lymphatic leukemia is so commonly observed as to lead to the suspicion that lymphatic leukemia may sometimes be of tuberculous origin. The present case, especially the structure of the cervical lymph nodes, the widespread lymphoid hyperplasia, the lesions of the liver, and the blood picture, lends some support to this view.

The distribution of tubercle bacilli was peculiar. They were found only in the necrotic areas, but not in any of the extensive areas of lymphoid infiltration. The results showed that they were present in the circulating blood. While cultures of the blood on ordinary media were negative, inoculation of 5 c.c. of the blood drawn December 13 into the superficial vein of the groin of a Rhesus monkey was followed by the death of the

animal in three months with acute general tuberculosis and a human tubercle bacillus was isolated from the organs by culture. We believe that intercurrent tuberculous infection of our monkeys can be eliminated. They were all recently imported, and three of the lot that died from enteritis within a few days of their receipt were entirely free from tuberculosis.

In morphology the bacilli were unusually long, and many much elongated and numerous branching forms were seen in sections. Since these branching forms stained with methylene blue they were at first regarded as streptothrix. They were, however, strongly acid-fast. An intensified Gram stain, as used by Much, gave more bacilli than carbol-fuchsin, but not in any new situations. In the lymphomatous areas it was not possible to find any Gram-positive granules that might be identified as derivatives of tubercle bacilli. The bacillus proved to be of the human variety, on morphology, because of its strongly acid-fast properties and its long, beaded and branching form; on cultural characters, as it grew luxuriantly on egg medium, produced a pellicle on broth in about three weeks, and the culture on egg developed a distinct pink color; and on biological features, failing to kill rabbits in six months, frequently proving fatal to guinea pigs, and causing acute general tuberculosis in Rhesus monkeys. Its acid production has not yet been determined.

The most striking clinical feature of the case was the extensive purpura which appeared shortly after the first symptoms and persisted with increasing intensity until the termination of the disease. Yet the occurrence of extensive purpuric eruptions in the course of tuberculosis has long been recognized, although in current text-books its importance is much underestimated. Thus Bensaude and Rivet, in 1906, gave a very full account of the relation of purpura and tuberculosis, drawing extensively from journals and text-books of fifty years ago; but in Osler's System, in an otherwise able review of purpura, the reader draws the impression that tuberculosis is practically a negligible factor in the etiology of purpura.

Bensaude and Rivet state that general purpuric eruptions occur, *first,* as a premonitory symptom of tuberculosis; *second,* in the course of acute or chronic tuberculosis; *third* in latent pulmonary tuberculosis; and *fourth,* with extrapulmonary lesions.

There is an extensive literature on the subject of tuberculous purpura, illustrating all of these relations.

(a) The premonitory form is well illustrated by a case of Mollière's, a man of twenty years, without tuberculous antecedents, who suffered for six weeks from joint pains and general purpura, before the appearance of cough, hemoptysis, and progressive pulmonary lesions ending in death one month later. Very similar cases are reported by Cohn, Wiechel, and Moizard and Grenet, the afebrile purpura preceding by one or two weeks, an acute pulmonary phthisis. In a case of Carnot and Harvier severe purpura of three weeks' duration disappeared and the patient seemed well, when pulmonary signs suddenly developed and cavities formed in six weeks. In a case reported by Hoke, a woman of fifty-nine years, previously quite well, suddenly developed a universal punctiform and macular purpura without fever. Two weeks later she died suddenly from cerebral hemorrhage. Autopsy showed acute miliary tuberculosis of the kidney and pelvic lymph nodes. In Herzog's case, a boy, whose parents were tuberculous, began to have attacks of purpura at four and one-half years of age, which were frequently repeated during seven years, when in his eleventh year he developed acute pulmonary phthisis which was rapidly fatal.

(b) In the majority of cases the purpura has marked a severe or fatal exacerbation of pulmonary tuberculosis, as reported by Bensaude and Rivet, Wagner, Bauer, Pratt, and others. In Pratt's case, a sailor, twenty-five years of age, duration of disease three months, general and increasing purpura hemorrhagica existed during the last seven weeks. Besides a general tuberculosis of lungs and spleen, with gastric ulcers, there was marked enlargement and caseation of many lymph nodes throughout the body.

(c) The relation to latent tuberculosis is illustrated by a

case of Dumas', of a soldier who suffered from punctiform purpura for several days and then suddenly died from cerebral hemorrhage. Autopsy revealed old tuberculous pleurisy and peritonitis. In many of the premonitory cases there is doubtless a latent focus which serves as a source of general infection, as in several cases collected by Bensaude and Rivet, and Carnot and Harvier.

(d) Purpura hemorrhagica has occurred in the course of many extrapulmonary lesions, as in the following cases quoted mostly from Bensaude and Rivet. With acute tuberculous meningitis (Troisier, 1873); in tuberculous orchitis (Gossner); tuberculosis of kidney and pelvic lymph nodes (Hoke); with tuberculous mesenteric nodes (Achmeticew); or cervical nodes (Kissel); or bronchial nodes; and with chronic coxitis (Fox). In a case of Vollbracht's, eleven months after a severe purpura, signs of Addison's disease appeared and autopsy showed tuberculosis of the adrenals.

It thus appears that severe general hemorrhagic purpura occurs under many conditions in connection with tuberculosis, and that it usually indicates an exacerbation of the tuberculous process. While ranking among the relatively rare manifestations of the disease its occurrence is sufficiently frequent to deserve more attention than it receives in current literature.

Many theories have been suggested for the pathogenesis of tuberculous purpura, from a constitutional hemorrhagic diathesis to acute bacteremia.

Although Rosenberger's results of finding bacilli in the blood in all of 125 cases of tuberculosis have not been verified, it has been fully proven by many observers that tubercle bacillemia is very common. The infectivity of the blood was shown by Veuillemin in 1866, and Weichselbaum found bacilli in the cadaver blood of several cases. In 1905 Jousset, by inoscopy, demonstrated tubercle bacilli in the blood in eleven of thirty-five cases (31 per cent) of acute and chronic phthisis. Liebermeister often found tubercle bacilli in the blood in pulmonary phthisis, and showed that this bacillemia is not of unfavorable prognosis since

it is not often followed by general miliary tuberculosis. Recently, 1910, Jessen and Rabinowitsch found bacilli or Much's granules in the antiformin sediment of nine out of thirty-six cases of tuberculosis, and they agree with Liebermeister that it is not of unfavorable prognosis. In view of these observations it would not be unreasonable to assume that tuberculous purpura is associated with sudden access of tubercle bacilli into the blood stream. Yet the occurrence of purpura in so many cases in which no general tuberculosis followed repeated attacks, and its complete disappearance, as in Gossner's case after extirpation of a tuberculous testicle, and the peculiar distribution of the petechiae in many cases, indicate that the lesions result chiefly from the action of toxic substances produced in the course of the disease. In the present case the histology of the petechiae showed nothing suggestive of the presence of bacilli.

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PRESENTATION OF A CASE OF CYSTICERCUS CELLULOSAE (?) OF THE FOURTH VENTRICLE.

CHARLES NORRIS, M.D.

The case was that of an Italian of thirty-five years. Since his immigration to this country, five years ago, he had always lived in New York City. Two months before his admission to Bellevue Hospital, in the service of Dr. James Alexander Miller, to whom I am indebted for the clinical history, he began to vomit after meals, the vomiting becoming more constant; and headaches set in, which became more and more severe. On admission the patient was fairly well nourished; there was constant vomiting and severe headache. Ophthalmic examination of the left eye showed a choked disc. The other eye examination was unsatisfactory. He was reported by the orderly to have died suddenly, several days after admission.

At autopsy, the convolutions of the brain were found markedly flattened, and with considerable distention of the cisternae at the base. The lateral and third ventricles were distended with clear fluid. On opening the roof of the fourth ventricle, a group of vesicles, composed of three cysts, the largest 5 x 7 mm., was found attached by a delicate pedicle to the wall of the fourth ventricle in its upper and lateral portion near the iter. There was considerable thickening of the ependyma of the iter and marked proliferation of the pia in the lateral processes of the fourth ventricle. A long worm, which was identified as *Tænia solium*, was found in the jejunum. No other noteworthy lesions except a chronic gastritis were found.

It is conceded that *Tænia solium* is the worm which infects man with cysticercus. The portal of entry is the intestine, as in this case. The ripe eggs entering the stomach during the regurgitation following vomiting (or a segment of the worm itself) are dissolved by the gastric juice, and the worm is set free from its shell and then penetrates the wall of the stomach. This mode of "auto-infection" of the worm was thought by Bruns to be the usual way in which a human being was infected. In only four of the seventy-two cases of cysticercus in the fourth ventricle, reported by Stern,[1] was a worm found in the intestine. Virchow, and practically all other authorities, believed that the infection occurs through the ingestion of uncooked meat or unwashed salads, etc. Owing to the habit of eating uncooked meat, the so-called "Finnen-krankheit" was very prevalent in Germany, before the meat inspection laws were in force.

Virchow reported that before 1885 one out of thirty-one bodies was infected by cysticercus. Henneberg's statistics (1903), compiled since the inspection laws were enforced, found the percentage of infected cadavers to be only 0.16 per cent. in Berlin.

The most interesting feature about the cysticercus disease of the fourth ventricle is the clinical history. The symptoms that are almost invariably present are headache, vertigo, and vomiting.

[1] Ueber Cysticerken im vierten Ventrikel. Arthur Stern. *Zeitschrift für klin. Medizin*. Bd. 61, 1907, pp. 64-121.

In 11 per cent. of the cases collected by Stern there were no symptoms. The disease has usually been diagnosed as tumor or hysteria, on account of the intermittent character of the symptoms. The cardinal point of diagnosis is that described by Bruns (1902), viz., the relationship of attacks of dizziness and of sudden death to sudden movements of the head.

The case was reported before sections of the cyst and its absolute identification had been made.

Dr. Norris also called attention to a second case, a gross specimen from a man sixty-seven years of age showing a tumor of the pituitary gland, probably an adenoma, without acromegaly.

Discussion :

Dr. J. H. Larkin said that at one of the meetings of the Society last year he had presented a very remarkable specimen of cysticercus of the brain. It should be remembered, however, that a great many of the cases of cysticercus cellulosæ of the brain were accidental findings, and that no diagnostic or pre-diagnostic condition had been discovered. Bruns, in an article which is one of the best on the subject, had gone into some detail as regarded the diagnostic or pre-diagnostic condition of the individuals who might have a predisposition to such an infection. Dr. Larkin said further that cysticercus of the brain was generally in the fourth ventricle, and that the dilatation might reach an enormous size. The specimen to which he referred was ten or even fifteen times as large as the one presented by Dr. Norris. They were of identical morphological type, i. e., three or four cysts closely connected by a small pedicle. The great majority of cases (in fact all of those reported by Bruns, and Dr. Larkin's) had been cases of sudden death. Dr. Larkin had also presented at the meeting referred to the brain of a monkey dying from cysticercus cellulosæ. In the monkey, the cysts were generally scattered throughout the cortical substance, and were not found in the cavities of the brain.

Dr. Coplin spoke of a similar case, reported by Dr. Lloyd. He had not reviewed his notes, and remembered merely the more

striking features. He recalled the fact that there were a large number of cysts in one of the lateral ventricles and a few collapsed sacs. The patient, who was said to have had some mental defect, maintained that with movements of his head he could feel things move about within. At autopsy it became evident at once that in the dilated ventricle not fully occupied by the cysts they might have floated forward or backward, and that the sensation complained of by the patient was in harmony with the anatomic findings. Dr. Coplin also recalled that there was considerable distention of the ventricles, together with very marked flattening of the convolutions, due, of course, to the distention. He did not remember, however, whether death had been sudden, or whether there were any other pathological findings of note.

Dr. H. W. Cattell said that he had had among his series of autopsies one case of cysticercus cellulosæ of the brain (1897). The death was sudden and the case was brought to the coroner's office as one of hydrophobia, the man having been bitten by a dog six weeks previously, the dog, however, presenting no signs of rabies. Briefly, the history was that of a man, aged twenty-three years, the autopsy revealing marked edema of the lungs and throat induced by chronic nephritis and cardiac failure. The brain was edematous and showed the presence of a number of cysticerci cellulosæ in a good state of preservation. The majority of these cysts were found in the sulci in the neighborhood of the larger blood vessels derived from the anterior, middle, and posterior cerebral arteries, while a few of the smaller ones were embedded in the brain substance, thus showing a wide distribution. No cysts were found in the ventricles. The man was a German, both by birth and in his manner of living. Dr. Coplin had reported from an examination of the medulla and cord that these parts did not show any evidence of hydrophobia.

A TUMOR OF THE NECK, SHOWING UNUSUAL HISTOLOGICAL FEATURES.

J. E. WELCH, M.D.

Case History: A. B. Confinement No. 17762. Age thirty-two; born in Ireland, Para 5; admitted to hospital May 20, 1910, presenting a condition of paraplegia and swelling on the right side of the neck. History as given by the patient was as follows:

During the latter part of a previous pregnancy, which was two years before admission, she noticed a small painless swelling on the right side of the neck, which varied in size from time to time, but was never tender. After the birth of this child, the swelling for a time grew much smaller, and then later increased gradually over a period of about one year, when she became pregnant again. During this last pregnancy the enlargement grew steadily until the time of death. About the middle of February, 1910, the patient was seen by Dr. Adolph Reich in her home. Dr. Reich gives an account of having found the patient at this time sitting in a Morris chair and unable to use her legs in any way. The history was not gone into carefully at this time, but the patient said she had been confined to her chair for several weeks, being unable to lie down on account of substernal pain, which always came when she assumed a reclining position. At this time she was about five and a half months pregnant. She was later advised to enter the hospital, which she did May 20, 1910. On admission to the Lying-In Hospital she was found to be between eight and nine months pregnant, appeared anemic and presented a tumor on the right side of her neck about the size of a hen's egg. Blood count on the day following admission showed 3,880,000 red cells, hemoglobin 78 per cent., 11,600 leucocytes, and a differential count as follows:

Small lymphocytes	10.	per cent.
Large lymphocytes	1.5	per cent.
Polynuclears	88.	per cent.
Eosinophiles	0.	per cent.
Transitionals	.5	per cent.

Urine analysis on this same date showed the following: Acid, deep amber, specific gravity 1,105, trace of albumin, trace of acetone, urea 0.9 per cent., no excess of indican; few pus cells and epithelium.

On May 24 the leucocyte count was as follows:

Total number of leucocytes........12,000
Small lymphocytes......... 5. per cent.
Large lymphocytes......... 4.5 per cent.
Polynuclears .... 89. per cent.
Eosinophiles .... 1.5 per cent.

For the first five days after admission the patient's temperature was in the neighborhood of 100°; on the sixth day she had a chill and her temperature rose to 105°; on the seventh day she was delivered of a premature child. From that time on until death her temperature fluctuated between 104° and 100°, several times reaching 105°. Two days just preceding death her temperature was subnormal, below 96°.

The question that presented itself to the surgeon in charge of this case was the possibility of relieving the paraplegia by laminectomy and removal of the growth from the spinal canal. The inference was that this pressure was due to a secondary deposit from what was considered the primary growth in the neck, which was thought to be lymphosarcoma, tuberculous adenitis, or Hodgkin's disease. In order to determine its exact nature, several laboratory tests were applied as follows.

Having first in mind lymphosarcoma, the Crile hemolysis test was made but proved negative; the von Pirquet test was then applied twice and proved negative both times. At this time the sputum was also examined, but no tubercle bacilli were found. Lastly, a Wassermann reaction was tried with a negative result.

At this time it was decided to remove under cocaine a small piece of the enlarged gland. This was done, and the specimen was sent to the laboratory for diagnosis. Microscopic sections of this tissue showed a lymphatic structure surrounded by a normal fibrous capsule. The lymph follicles in the central part of the tissue showed hyperplasia of the lymphoid cells. Towards the

periphery of the gland there was an extensive formation of very dense hyaline interstitial fibrous tissue. This was especially marked beneath the capsule and was less dense as the center of the node was approached. The section appeared to present a simple inflammatory condition. Not being satisfied with this report, another piece of the tumor was asked for and received a few days later. Sections through this tissue showed changes as above described, i. e., extensive formation of interstitial hyaline fibrous tissue peripherally and lymphoid hyperplasia centrally. The lymph cells showed no tendency whatever to penetrate the capsule, but, instead, where this process might be expected, a fibrous condition was found. This second specimen showed, however, in addition, scattered through the hyperplastic lymph follicles a few giant cells having large oval nuclei placed centrally and rather small cell bodies. The association of these peculiar giant cells in the hyperplastic lymphoid follicles with a tendency to form interstitial fibrous tissues at the periphery of the gland led to the deduction that the process was an inflammatory one and of the nature of a granuloma, hence the diagnosis of Hodgkin's disease was made. After removal of the sections for microscopical examination, the patient's condition grew gradually worse, the anemia increasing, and the tumor in the neck enlarging. About three months before the patient died, a small tumor appeared on the left side of the neck, but did not grow very large.

Post-mortem examination (made by Dr. Douglas Symmers) —Inspection shows the body of a woman, poorly nourished, skin and visible mucous membranes very pale; on the right side of the neck a tumor mass measuring about 1 cm. in length and 3 cm. in breadth, with its long axis running parallel with the long axis of the neck. The mass is coarsely lobulated, slightly movable against the deeper structures, but attached to the skin. Over the lower part of the tumor is a small surgical scar well healed. The supraclavicular lymph nodes are palpable. The axillary, epitrochlear, and inguinal nodes can not be felt. The lower limbs are flexed at the knees at an angle of 135 and can

be straightened only with difficulty. Both heels present blackened decubital ulcers. The post-tibial tissues at the lower third of the leg are markedly edematous. In the sacral region is an enormous irregularly outlined decubital ulcer. The edges are thickened and the base is made up of underlying bony tissue which is discolored and ill-smelling. Several bony prominences, including the posterior spine of the ischium and the head of the left femur are freely exposed.

Brain—On removing the dura mater, a minute rounded metastasis on the right side comes into view. The brain is small, sulci are deep, convolutions are narrow and atrophic. On section, no noteworthy appearances are observed.

Spinal Cord—On opening the medullary canal, a collar of tissue corresponding in all naked eye essentials to that described in the neck and abdominal lymph node comes into view around the mid-dorsal cord, between the sixth and eighth dorsal vertebrae. On removing the cord and opening the meninges, this tumor mass is found to be entirely extradural. The underlying cord, however, is small and shows evidences of compression. On section the mid-zone of the cervical cord on either side presents considerable brick dust discoloration. In the dorsal cord no definite changes are visible to the naked eye.

Thorax—The thymus is absent; diaphragm normally placed; dense adhesions posteriorly in both pleural cavities; pericardium is normal; the heart is small, brownish yellow in color and flabby, shows no special pathological change. The lungs show moderate emphysema only. Immediately beneath the pleura near the hilum of the left lung is a small flattened pale mass which, upon section, presents a pale, smooth, rather translucent appearance. It extends downward into the parenchyma for a short distance. On removing the tongue, larynx, thyroid and upper esophagus, the tumor mass previously described on the right side of the neck is partly dissected out and removed. It appears to spring from the regional lymph nodes and to bear no connection with the periosteum of the jaw or spine. It fills in the neck from the level of the skull almost to the clavicle and lies close to the side of

the spine. It is made up on section of innumerable rounded or oval bodies which are firmly bound together, and present a perfectly smooth, pale, translucent, glistening surface, the substance of which is firm in consistency. Occasionally yellowish, apparently necrotic areas are present in the cut surface.

Spleen—Is considerably enlarged, and the capsule is tense; it has a diffuse steel-blue color. Close inspection of the cut surface shows numerous areas of amyloid degeneration.

Liver—Is greatly enlarged; lower border of the right lobe reaches the level of the umbilicus. This organ is yellowish in color, the surface is smooth, lobules are well differentiated; no focal lesions or amyloid are found.

Pancreas—Unchanged.

Adrenals—Unchanged.

Kidneys—Left, surrounded by considerable fat; on section the organ cuts readily. Capsule strips readily, leaves behind a surface which in places is greyish red and smooth, but in other places is studded with pin-head to bean sized, cream colored bodies which release soft pus when the capsule is reflected from them. The cortex is, for the most part, very pale, bulges greatly beyond the cut edge of the capsule, and is poorly differentiated from the medulla. Scattered through the cortex and medulla of the lower third of the organ are innumerable points and streaks made up of pus. The mucous membrane of the pelvis is swollen, pale, and opaque. The right kidney is essentially like the left.

Bladder—Small; walls are greatly thickened; mucosa is diffusely reddish, very opaque, and markedly swollen and edematous. At one point is a small collection of pus lying immediately beneath the surface.

Uterus—Shows no changes.

Gastrointestinal Tract—Shows no lesions.

Peritoneum—Shows no change.

Abdominal Lymph Nodes—At the lower end of the spine on the left side near the sacro-iliac synchondrosis are numbers of enlarged lymph nodes which upon section present essentially the same naked eye appearances as those described in the neck,

but with the addition of numerous minute reddish points in the cut surface.

Microscopic sections through the primary tumor in the neck, the nodule in the lung, and the growth in the spinal canal, all show a similar structure which is very different from the picture presented by the sections examined ante-mortem. There is a very extensive production of fibrous tissue which is very dense, has a hyaline appearance for the most part, and has a retiform arrangement through the growths. The interstices of this fibrous tissue framework contain a very great variety of cells. There are numerous very large multinuclear and uninuclear giant cells. None of these giant cells resemble in any way those found associated with tuberculosis or syphilitic lesions. Their nuclei are not arranged peripherally, but are found in the center of the cells, usually overlapping each other and occasionally having a roseate appearance. There are also found numerous very large cells with dense protoplasm staining deeply by eosin with dense chromatin nuclei, many of which show mitotic figures. There are a few plasma cells scattered here and there, and an occasional eosinophile. The lymphoid tissue has been almost entirely replaced. A few cells only remain to indicate its former presence. Superficial examination of these tumors might lead to the conclusion that the growth was sarcomatous, but consideration of the ante-mortem histological appearance and the tendency to fibrous tissue proliferation rather than new cell formation, inclines one to the conclusion that the process belongs to the class of granulomata. This conclusion is also favored clinically by the long duration of the disease, and the lack of a tendency rapidly to infiltrate surrounding structures which is one of the marked characteristics of sarcoma. Microscopically, we find everywhere marked tendency to the production of interstitial hyaline fibrous tissue, which is true especially about the periphery of the growths, a situation where in sarcoma we expect to find a very cellular structure instead of a fibrous one.

I wish to present this as a case of Hodgkin's disease with unusual histological changes late in the disease.

Average Count in All Cases of Dr. Reed.

Red blood cells 3,829,000
Hemoglobin ...... Per Cent.   56
Leucocytes 11,563

Differential:

	Per Cent.
Small lymphocytes	19.5
Large lymphocytes	5.2
Polynuclears	57.2
Eosinophiles	2.3
Transitionals	2.8

Highest Count, Dr. Reed.

Red blood cells 5,264,000
Hemoglobin ...... Per Cent.   84
Leucocytes 15,500

Differential:

	Per Cent.
Small lymphocytes	36.8
Large lymphocytes	11.5
Polynuclears	84.28
Eosinophiles	5.
Transitionals	7.8

Lowest Count. Dr. Reed.

Red blood cells 2,670,000
Hemoglobin ...... Per Cent.   51
Leucocytes 6,200

Differential:

	Per Cent.
Small lymphocytes	2.
Large lymphocytes	.8
Polynuclears	46.4
Eosinophiles	.05
Transitionals	.6

Average of Three Counts in This Case.

Red blood cells 3,890,000
Hemoglobin ...... Per Cent.   77.5
Leucocytes 11,800

Differential:

	Per Cent.
Small lymphocytes	7.8
Large lymphocytes	5.4
Polynuclears	85.6
Eosinophiles	0.5
Transitionals	1.

Highest Count, This Case.

Red blood cells 3,900,000
Hemoglobin ...... Per Cent.   78
Leucocytes 12,000

Differential:

	Per Cent.
Small lymphocytes	10.
Large lymphocytes	10.2
Polynuclears	89.
Eosinophiles	1.5
Transitionals	1.2

Lowest Count, This Case.

Red blood cells 3,880,000
Hemoglobin .... Per Cent.   77
Leucocytes 11,600

Differential:

	Per Cent.
Small lymphocytes	5.
Large lymphocytes	1.5
Polynuclears	79.8
Eosinophiles	.2
Transitionals	....

Discussion:

DR. JAMES EWING said that he had had the pleasure of looking at the specimens exhibited by Dr. Welch, and considered them one of the most interesting sets of specimens of Hodgkin's disease that he had ever seen. He had been in the situation of seeing a structure which he and, he thought, most pathologists were in the habit of regarding as large round cell sarcoma, but which in fact was not a true sarcoma. He agreed with Dr. Welch that the case was not a lymphosarcoma, and thought, on account

of the features brought out by Dr. Welch, that it was in all prob-
ability a case of Hodgkin's disease. The tumor itself did not
show the gross characters which must be demanded of a malig-
nant lymphoma. It did not show the local destructive and in-
vasive capacities of a lymphosarcoma. Nevertheless the micro-
scopical structure of the tumors in the spinal dura, in the lung,
and in the liver, had strongly impressed several pathologists as
certainly sarcoma. The question naturally arose: "Under what
conditions would one be justified in entering a diagnosis of sar-
coma of the lymph nodes?" In this case the rich chromatin
content of the cell nuclei of true lymphosarcoma was lacking.
Dr. Ewing added that the difference of opinion which had arisen
concerning the nature of this case had resulted, in part, because
Dr. Welch, who could not perform the autopsy, had not received
portions of all the material, while those who had examined the
autopsy material had not had the benefit of seeing the sections
of the node removed some months before death. He thought
that the lesions in the spinal dura, liver, and lung, were strongly
suggestive of sarcoma, while the sections of the lymph nodes in
Dr. Welch's possession, especially that of the node first removed,
seemed to show clearly that the case was one of Hodgkin's dis-
ease. Apparently the character of the process had changed, as-
suming, in some of the secondary lesions, some of the characters
of a neoplasm. Dr. Ewing thought it still doubtful whether one
would be justified in calling the later lesions true sarcoma.

Dr. W. G. MacCallum had also seen Dr. Welch's speci-
mens, but was forced to admit that he could not yet say what
the case was, except that it did not correspond to Hodgkin's dis-
ease, unless it was by the greatest stretch of the imagination. Dr.
Welch had, moreover, gone to considerable pains to prove that
it did not invade the surrounding tissues; but how, then, did it
get into the spinal canal? Dr. MacCallum agreed with Dr.
Ewing that the tumor did not resemble lymphosarcoma, and that
it had not the histological character of a lymphosarcoma. He
was of the opinion that it resembled those sarcomata arising in
the retroperitoneal region, in which there are large cells of multi-

nuclear character, often with very large nuclei and mitotic fig-
ures, which sometimes grow very rapidly and sometimes slowly.
On the whole, Dr. MacCallum thought that the case under dis-
cussion was one of a neoplasm of slow growth.

DR. KARSNER thought that the case was of interest, espe-
cially in view of the publication of two cases by Yamasaki in
1904 (*Ztschr. f. Heilk.*, xxv, 269) which seemed to be of a sim-
ilar nature. Yamasaki believed that these cases were primarily
Hodgkin's disease with sarcomatous transformation. Dr. Kars-
ner had published a case in 1910 (*Arch. Int. Med.*, vi, 175)
similar to those of Yamasaki. All of these seemed to be similar
to Dr. Welch's case. The condition when it appeared as a new
growth was richer in cells than when it occurred in the lymph
nodes, showed more giant cells, more large mononuclears, more
leucocytes, and fewer lymphocytes, and was definitely invasive.
Dr. Welch's case fulfilled these conditions, and it seemed to Dr.
Karsner that the case was one of Hodgkin's disease, which had
metastasized as an independent neoplasm. This view presup-
posed the acceptance of the assumption that Hodgkin's disease
is a granulomatous condition.

DR. WELCH concluded the discussion by saying that the
metastasis was what one would expect in Hodgkin's disease, in
that it affected only previously existing lymph nodes which might
be anywhere in the body. Dr. Osler had reported a case of para-
plegia due to Hodgkin's process in the lymph node in the spinal
canal. A superficial examination of these tumors would lead
to the conclusion that it was not a case of Hodgkin's disease,
but a sarcoma; yet, if he had occasion again to make a diagnosis
of a case like this, he would undoubtedly pronounce it a case of
Hodgkin's disease. He was of the opinion that a careful study
of the development showed that it was not a truly malignant
growth, but belonged in the class with the granulomata.

RICKETS.

W. G. MAC CALLUM, M.D.

The disease occurs in different forms in different regions; in some cases there is enough atrophy of the bone to allow of bending at the center and throughout the diaphysis; in others there results a sharp bend in the osteoid tissue at the epiphyseal line. The changes are like those of osteomalacia in certain respects, e. g., the softening and atrophy by way of the production of osteoid substance. The distinction lies in the existence of endochondral changes in rickets which result from its occurrence in the age of maximum growth acitvity.

The changes in the bones of rickets are essentially three:

1. The periosteal growth of new bone and osteoid tissue.
2. The endosteal growth of new bone and osteoid tissue.
3. The endochondral changes.

1.—In many cases there is extensive osteophyte production, thought by some to be compensatory in nature, by others to be set up by the tension of the attached ligaments and tendons. This tissue is similar to the periosteal growth in callus formation, but is relatively slightly calcified, i. e., consists principally in the formation of osteoid.

2.—In the marrow, in relation to the endosteum, there is a change in the tissues (endosteitis fibrosa, osteomyelitis fibrosa) which gives the content of the interlaminar spaces a fibrous character. Laminæ of bone or osteoid tissue are formed by the activities of this tissue, either by the transformation of the fibroid cells into osteoblasts, or by a direct metaplasia. Most of the laminæ may be only partly (centrally) calcified and remain as osteoid.

In both these cases the essential question is as to the production of the osteoid substance—is it a calcium-free apposition, or is it the result of absorption of the calcium salts from the old finished bone laminæ? This question is particularly difficult when the laminæ concerned are in a position (c. g., in the cortex of the shaft) where they may well consist of altered old bone.

M. B. Schmidt is thoroughly in favor of halisteresis and adduces as arguments the existence of calcium-free portions of an otherwise complete and well-calcified Haversian system, the existence of calcium-free ends of lamellæ for a short distance about perforating canals where the rest of the lamellæ are calcified, and, further, the very rapid calcium loss which occurs in the production of such changes. He lays little stress on the "*Gitterfiguren*" of v. Recklinghausen. Marchand supports this view in that there are laminæ with central calcification which, if not formed by halisteresis, must have hung perfectly free in the marrow cavity and there been added to by apposition. Others (Pommer, Schmorl) support the idea of calcium free apposition. Dibbelt rather leans to halisteresis, but the question is far from settled.

3.—The endochondral change characteristic of rickets is found to happen in the following way: at first the invasion of the cartilage by blood vessels is essentially from the marrow cavity, and since calcification of the cartilage, normally present but provisional, occurs in this disease to a far less degree and in irregular areas only, the vessels grow far and branch into the cartilage where it is not calcified, but are restrained where it is. Soon in the florid stage this ingrowth fades into insignificance as compared with the invasion of perichondral vessels from all sides. These arteries and veins which lie in the cartilage marrow canals, grow horizontally and form layers with downgrowing capillaries which later anastomose with those from the marrow cavity. If there are remissions, several such "stages" may be formed. About such vessels there is a sheath of fibrous tissue, and the adjacent cartilage which stains bluish normally, begins to take a pink stain (possibly because of the exchange of a collagenous material for its original chondrin content) and with slight changes in the form of the cells, it assumes the characters of osteoid tissue, a metaplastic process which quite regularly converts whole peninsulas of cartilage into osteoid. Some of the cartilage is simply calcified, and little of it, perhaps none, is converted into real bone in the florid stage of the disease. The enlargement of the epiphyses is due not so much to any excessive

production of cartilage as to the fact that it does not become converted into the calcified and less bulky bone.

As to the other organs in rickets, there is no unanimity of opinion. In most cases the spleen is enlarged and there is marked anemia, but this is not held to throw any light upon the pathogenesis of the condition. On the other hand, Stoeltzner attributes the whole change to insufficiency of the chromaffin system, and thinks the lack of adrenalin secretion the fundamental factor in its production. This idea he bases on the observed resemblance to Addison's disease in the atony or hypotony of the skeletal muscles as well as of the smooth muscles of the intestines and arteries. The inadequacy of the adrenalin secretion may be due to the inactivity of the child, for he conceives muscular movements to be necessary to squeeze out the adrenal secretion. Indeed, there have been striking therapeutic effects obtained in osteomalacia by the injection of adrenalin, but their interpretation is not yet quite clear. Similarly Fehling has advanced the theory that the ovaries are in some way responsible for these changes and has produced remarkable cures by their extirpation, but his arguments are easily attacked. Both insufficiency and hyperactivity of the thyroid have been regarded in the same light as causative factors, but on insufficient grounds, and possibly the same may be said for the parathyroids.

In the case presented all of the organs of internal secretion were examined and demonstrated in microscopical preparations, but in none of them could any obvious lesion be seen. Nevertheless it still seems possible that one or other of them may be responsible for the fundamental change in rickets, which is after all not a primary alteration in the nature of the bone, but an inability to make use of the calcium furnished for the process of ossification. It is not as was thought, an excessive production of osteogenic tissue, but rather a retardation or stagnation of the normal bone formation resulting from incapacity to use the calcium supplied.

Studies of metabolism have so far led to quite indefinite results, but whether or not it is greatly increased, the excretion of

calcium in rickets is exclusively by the intestine, and Dibbelt puts
forward the idea that decomposition products in the intestine
withdraw calcium from the blood by producing an insoluble cal-
cium compound within the intestinal lumen.

Discussion:

Dr. Riesman, in discussing Dr. MacCallum's case, said that
it was strange that so little should be known of the etiology of a
disease that had been studied for so long. Dr. MacCallum had
indicated very clearly the pathological anatomy of rickets. The
essential change in the disease, as the researches of Pommer and
Schmorl showed, was one of deficiency of lime salts. Not alone
was the new bone deposited without a proper quantity of calcium
salts, but there was a coincident resorption of mineral salts from
the existing bone. In some instances, in addition to the changes
found by Dr. MacCallum, there had been more or less charac-
teristic alterations in the voluntary muscles. Regarding the true
cause of rickets, the speaker said we were no wiser than in the
days of Glisson, two hundred and fifty years ago. It was almost
amusing to see what varied agents had been blamed for the dis-
ease. Some writers looked upon the cause as nutritional, the
fats, the proteids, the carbohydrates, and the salts having in turn
been accused. Bland and Sutton's experiments seemed to point
to diet as an essential factor. Lion whelps fed by him on raw
meat and rice developed rickets, but they were cured when milk,
pounded bone, and cod liver oil were added to the dietary. The
recovery of the lions took place although no change was made in
their environment. Monkeys on a purely vegetable diet also
became rachitic. Similar observations had been made by Guerin
on puppies. It had been held on the strength of the experiments
detailed that rickets occurred in the animals because the food
was deficient in lime salts. The speaker did not think that such
a deficiency could be the cause of rickets. Rickets had occurred
in children at the breast of mothers whose milk had been found
to contain an abundance of lime salts. Confinement, lack of
sunlight, domestication, had something to do with the develop-

ment of the disease, for, as Holt had shown, the Italian children
became rachitic in New York, but not in their native home.
Rickets had also been produced in puppies by keeping them tied
and confined. Schmorl, one of the best students of rickets, was
of the opinion that it was caused by infection. Morpurgo, an
Italian, claimed to have produced the disease in young animals
by the injection of a diplococcus. As to the adrenalin theory,
the speaker hardly thought that the suprarenal gland was at
fault. Moreover, Dr. MacCallum had just shown that neither
the adrenal gland nor any other organ of internal secretion, was
diseased. Recently, however, therapeutic results from the ad-
ministration of suprarenal extract had been reported. The
speaker had lately seen a case of rickets in a child living under
ideal conditions. Though the disease was mild, there was a
rachitic rosary. It was evident that it was necessary to go further
to find the cause of the disease. He was glad that Dr. MacCal-
lum had brought the subject forward so that a new interest might
be taken therein, inasmuch as rickets had hitherto been treated
as a step-child by pathologists.

Proceedings

of the

New York Pathological Society.

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DR. RICHARD M. PEARCE. *President.*

A CASE OF MENINGOCOCCUS ENDOCARDITIS WITH SEPTICEMIA.

RUSSELL L. CECIL, M.D., AND WILLARD B. SOPER, M.D.

Patient, male, stage carpenter, age thirty-one years, ad-
mitted to the 2d Medical Division of the Presbyterian Hospital,
June 5, 1910, complaining of headache, pain in left arm and
chest, lassitude, and fever. Family history negative. Personal
history negative, except for immoderate use of alcohol. Patient
gave history of two attacks of rheumatism, the first one fifteen
years ago, the second, twelve years ago. He was confined to bed

several months during both attacks. He had gonorrhea five years ago. No history of lues.

Present illness: Two weeks before admission patient had a sore throat, felt feverish, and noticed some pain and tenderness in right wrist and elbow. Two days later he began to have severe frontal headaches, which continued up to the time of admission. He had vomited a number of times and had some diarrhea. In spite of these symptoms, he continued to work until four days before admission. At that time he began to have a dull pain across the whole anterior chest, which was not increased by the cough that now developed.

Physical examination showed a well nourished man, mentally clear, of good color, but much prostrated. Ear-drums normal. Left pupil larger than right, but both react normally. Tonsils moderately enlarged and congested, but without exudate. Neck not stiff. No enlargement of heart made out. Regular action 100 per minute. Presystolic and systolic murmurs can be heard at the apex. Lungs normal. Abdomen soft. Spleen not felt. No petechiae, no Kernig, no Babinski. Knee jerks sluggish. Right ankle somewhat swollen and painful on motion. On the third finger of the right hand, the metacarpo-phalangeal and first interphalangeal joints are swollen, red, and quite tender. Considerable coarse tremor of hands. Temperature 102.5°. Pulse 100. Respiration 32.

Clinical diagnosis: Rheumatic fever and endocarditis.

June 8: The patient's temperature rose to 104.5° and has maintained a level of 102-104.5°. Marked tremor of hands has developed. Patient is quite irrational. Symptoms and physical signs otherwise the same. Leucocytes, 15,000; 86 per cent. of polynuclear leucocytes. The picture is that of an extreme toxemia. The blood culture taken on the day after admission has been reported sterile. Widal reaction negative.

June 9: Patient delirious, with fairly marked subsultus. Leucocytes 12,000 with 90 per cent. polynuclear leucocytes. No petechiae. No signs of meningitis.

June 12: Temperature has continued on a level of 103-

104°. Pulse and respiration have slowly increased, and are now respectively 120-124 and 28-32. Clinically the patient has shown the picture of typhoid fever, except for the absence of rose spots and enlarged spleen. He lies semi-delirious the whole time, having considerable twitching and subsultus. Movements involuntary, but takes fluid greedily. Circulation has kept up well. Blood culture taken on June 9 gave a pure growth of a Gram negative diplococcus, which was reported as probably meningococcus. On the basis of that report patient was given 15 c.c. of Flexner's antimeningitis serum subcutaneously without effect. Patient has had no signs of meningitis.

June 15: Patient gradually failing. Temperature, pulse, and respiration are all rising. The blood culture on June 12 shows same organism found in previous culture. To-day patient received intravenously 15 c.c. of Flexner's serum. Lumbar puncture performed three days ago showed normal fluid. There are now for the first time a few petechial spots, size of pin heads, just beneath the left clavicle.

June 15: Temperature rose to-day to 106°. Delirium changed to coma. Some stiffness of legs and neck, thought not to be that of meningitis. Patient died to-night, circulation having steadily failed despite stimulation.

The autopsy was performed June 16, sixteen hours after death. Only the most interesting features will be referred to.

The body is that of a fairly well nourished young man, 176 cm. in length. Post-mortem rigidity is present. There is livor mortis in the dependent parts.

On opening the abdomen, the liver is found bound to the diaphragm by firm fibrous adhesions. With this exception, the abdominal cavity is negative.

There are old fibrous adhesions in both pleural cavities. The lungs are voluminous and heavy. Their cut surfaces are dark red and ooze considerable blood-tinged frothy fluid.

The pericardial sac has been partially obliterated by fibrous adhesions. The heart with pericardium attached, weighs 670 gms. and is considerably enlarged. The pericardium is peeled

off with difficulty, exposing a rough, ragged surface. The right side of the heart contains a post-mortem blood clot. The tricuspid valve measures 12.5 cm. in circumference, the pulmonary valve, 8.5 cm. The leaflets of both valves are normal. There is some hypertrophy of the right ventricle. The mitral valve measures 8.5 cm. in circumference. The two curtains are thickened and fused together so as to form a thick ring. On the auricular surface of the anterior curtain there is a soft cauliflower vegetation, 1.5 cm. in diameter. The base of the vegetation is firmly adherent to the valve leaflet. The aortic leaflets are thickened and pouched out. The free borders of the segments are retracted. The left ventricle is considerably enlarged The papillary muscles are hypertrophied. The musculi pectinati are somewhat flattened. The left ventricular wall measures about 2 cm. in thickness, and has a soft flabby consistence. The musculature is reddish brown and homogeneous. The coronary arteries are clear.

The spleen is large and soft; weight 590 gms. The capsule is smooth. The cut surface is dark purplish red, and has a velvety appearance. Considerable pulp comes away with the knife. The markings are indistinct. Along the anterior border there is a sharply defined pinkish-white area, which on section corresponds to the base of an irregular wedge, firm in consistence, and slightly elevated above the surrounding tissue.

The liver is large and rather soft and pliable. Weight 2,050 gms. The cut surface is pinkish-yellow and opaque. Gall-bladder and bile ducts normal.

The pancreas weighs 200 gms. with duodenum attached, and appears normal.

The right kidney weighs 190 gms. The capsule is somewhat adherent. The surface of the kidney is finely granular. The cut surface is cloudy and swollen, the cortex measuring 10 mm. in thickness in some places. At the upper pole, there is a small pale yellow area surrounded by a narrow zone of red. Section through this area exposes a firm wedge shaped mass of yellow tissue, surrounded by a dark red zone. The pelvis of the

kidney is dilated and contains a large rough stone, which sends off projections into the calices. The pelvic mucosa is injected, roughened, and covered with mucus. The right ureter is normal

The left kidney weighs 240 gms. It is finely granular and cloudy like the right. No infarcts occur. Left pelvis and ureter normal.

The suprarenals are normal.

The bladder and prostate are normal.

Nothing of interest is found in the gastro-intestinal tract. The aorta shows no changes. The larnyx and trachea are normal. The brain weighs 1450 gms. The dura mater is normal. The cortex is edematous, but translucent. The sulci contain clear serum. The base of the brain is free from exudate. The ventricles are normal. Frontal sections through entire brain show nothing of interest.

Microscopical sections from the organs showed the following:

Brain: Sections through the various parts of the cortex, as well as the pons and medulla, show a normal pia-arachnoid. Here and there a few lymphoid and plasma cells occur, but nothing suggestive of an exudate can be made out.

Vegetation on Mitral Valve: The vegetation is composed chiefly of fibrin, which in many places has undergone hyaline necrosis. Toward the periphery, the vegetation contains a large number of polynuclear leucocytes, many of them partially disintegrated.

Kidney: The epithelium of the convoluted tubules is cloudy and granular. At one point in the cortex the tubules and glomeruli have undergone a hyaline necrosis. Around this necrotic area, the veins and capillaries are intensely congested.

Spleen: The sinuses are filled with red blood cells. There is a large area of coagulation necrosis, throughout which a network of fibrin is seen. Just outside the necrotic area, there is a hemorrhagic zone. In several of the larger veins passing through the necrotic focus, fresh mural thrombi occur, some of them occupying half or more of the vessel's lumen.

Liver: Cloudy.

Pancreas: Normal.

Suprarenal: Normal.

Heart muscle: There is a slight increase of the interstitial tissue.

Lungs: Normal.

⊦ *Prostate:* Normal.

Anatomical diagnosis: Acute vegetative mitral endocarditis. Chronic mitral and aortic endocarditis. Mitral stenosis, hypertrophy and dilatation of heart. Chronic fibrous pericarditis. Chronic interstitial myocarditis. Chronic fibrous pleuritis. Congestion and edema of the lungs. Acute splenic tumor. Chronic interstitial nephritis. Nephrolithiasis. Anemic infarcts in spleen and right kidney. Cloudy swelling of viscera.

The bacteriological examination of the various organs gave the following: (1) Vegetation on mitral valve. Smears from the vegetation show red blood cells, fibrin, and leucocytes. In some of the leucocytes one to a half a dozen pairs of Gram negative diplococci are found. These organisms are biscuit shaped and show various stages of dissolution. Morphologically, they resemble in every way the diplococcus found in the blood cultures. A culture taken from the surface of the vegetation shows a few colonies of *B. coli communis.*

(2) Smears from the serous fluid beneath the pia mater show a few endothelial cells. No pus cells or diplococci can be found. Cultures from pia mater give streptococci and colon bacilli.

(3) Cultures from liver, spleen, and heart's blood show many colonies of *B. coli communis* and a few colonies of streptococcus.

(4) Smears and cultures from the prostate gland show no gonococci.

————————

In order to establish firmly the diagnosis of meningococcus endocarditis, it has been necessary to prove two premises: First, that the organism isolated from the patient's blood was a genuine

meningococcus: Second, that this same organism was instrumental in producing the vegetations on the mitral valve.

(1) Bacteriological study of the diplococcus.

(a) Morphology: The organism isolated from the patient's blood is a small biscuit shaped diplococcus, which does not retain the Gram stain. Morphologically, it resembles the gonococcus. The diplococci vary considerably in size and many involution forms occur.

(b) Cultural reactions: Subcultures, taken from the original broth flasks showed the following: On ascitic glucose agar, after twenty-four hours, there appeared a diffuse, grayish, translucent mucoid growth. On removing some of the growth with a platinum wire, it was seen to have a distinctly viscid quality. Subcultures in broth, plain agar, blood agar, glucose agar, litmus milk, and Loeffler's blood serum, all remained sterile. By making generous transfers, however, from the ascitic glucose agar culture, growths were obtained on all the serum media, and two weeks later the organism was successfully cultivated on plain and on glucose agar.

(c) Fermentation tests: The organism ferments glucose and maltose, but not lactose or saccharose.

(d) Pathogenicity: A guinea-pig was injected peritoneally with one-fourth of a twenty-four hour growth of the organism on glucose agar. It appeared sick on the following day, but completely recovered. This test of the organism's pathogenicity was not carried out until two weeks after its first cultivation on culture media.

(e) Agglutination and absorption tests: An emulsion of the organism in normal salt solution was prepared from a twenty-four culture on glucose agar. The proportion was 4 mg. of the growth to 1 c.c. of salt solution. Two stock strains of meningococcus were used for controls. The three organisms were tested with the serum from a rabbit highly immunized against the meningococcus. Equal parts of the emulsion and of the variously diluted serum were mixed in small test tubes and allowed to stand in the incubator at 37° C. for two hours. They

were then placed in the ice box for twenty-two hours. In the positive reactions a flocculent sediment was covered by clear supernatent fluid. In the negative reactions the emulsion remained homogeneous and opalescent. The following table shows the results obtained:

TABLE No. 1.

Organism	1–10	1–25	1–50	1–100	1–250	1–500	1–1000	1–2500	1–5000	1–10000	1–15000	Salt solution Control
Diplococcus J. S.	+	+	+	+	–	–	–	–	–	–	–	–
Meningococcus Duval.	+	+	+	+	+	+	–	–	–	–	–	–
Meningococcus 250.	+	+	+	+	+	+	+	+	+	+	–	–

Diplococcus J.S., the organism under consideration, was agglutinated by a 1-100 dilution of the serum. The first control strain of meningococcus was agglutinated by a 1-500 dilution of the serum; the second control, the homologous strain, was agglutinated by a much higher dilution, 1-15000.

In the absorption tests, a 1-5 dilution of the serum was first mixed with 1 c.c. of an emulsion of the organism, and the mixture incubated at 37° C. for two hours. Then, after thorough centrifugalization, the clear serum was decanted off, and various dilutions of it were tested with the organisms as in the original agglutination tests. In Table No. 2 the results are seen.

TABLE No. 2

ABSORPTION OF MENINGOCOCCUS IMMUNE SERUM

Organism	Agglutinative Titer with unabsorbed serum	Agglutinative Titer after absorption with Diplococcus J. S.	Percentage of agglutinins lost by absorption	Agglutinative Titer after absorption with Meningococcus 250	Percentage of agglutinins lost by absorption
Diplococcus J. S.	1–100	1–25	75%	1–25	75%
Meningococcus 250	1–15000	1–5000	66.6%	1–10000	33.3%

The table shows that, after absorption of the serum for two hours with diplococcus J.S., the agglutinating power of the serum was considerably reduced for both organisms. In other words, diplococcus J. S. has the power to absorb specific meningococcus agglutinins. Similar reductions in the agglutinative titer of the serum were observed after absorption with its homologous strain, "Meningococcus 250."

(f) Deviation of complement: In addition to the agglutination and absorption tests, we have also tried the deviation of complement test. The hemolytic system devised by Dr. Noguchi was employed. The antigen was prepared as follows: A twenty-four hour growth of the organism was washed from the surface of a glucose agar slant with 1 c.c. of normal salt solution. The emulsion was well shaken, covered with toluol, and allowed to autolyze over night in the incubator at 37° C. The toluol was then carefully removed, the emulsion centrifugalized, and the clear supernatent fluid pipetted off. For amboceptor we used antimeningococcus horse serum, which was kindly furnished us by Dr. Lamar of the Rockefeller Institute.

There was complete inhibition of hemolysis when 0.01 c.c. of antigen from diplococcus J.S., and 0.05 c.c. of the antimeningococcus serum, were used. With the control strain, inhibition occurred with a slightly smaller quantity of amboceptor, namely, 0.02 c.c. These tests were, of course, controlled with normal horse serum.

The organism showed all the morphological and cultural characteristics of the meningococcus. It was agglutinated by a 1-100 dilution of antimeningococcus serum; finally, it possessed the power of absorbing specific meningococcus agglutinins and of binding complement with specific antimeningococcus amboceptor. We feel justified, therefore, in concluding that the organism was a genuine meningococcus.

(2) Bacteriological Examination of the Vegetations.

In order to show that the vegetations on the mitral valve were caused by the meningococcus, we studied the smears and culture taken at the autopsy, and in addition have cut sections of

the vegetation and stained them for bacteria. The smears showed the characteristic Gram negative diplococci in the leucocytes. Only one culture was taken from the vegetation, and that showed a single colony of *B. coli communis*.

Examination of sections through the vegetation reveals many polynuclear leucocytes in a partially necrotic network of fibrin. In many of the leucocytes one to a half dozen pairs of Gram negative biscuit shaped diplococci can be seen. No streptococci can be found in any of the sections of the vegetation.

After having found streptococci in the cultures from the liver, spleen, and heart's blood, it occurred to us that perhaps, after all, we had been dealing primarily with a streptococcus endocarditis, and that the meningococcus was a secondary invader. A careful study, however, of the smears and sections taken from the vegetations have convinced us that the reverse is true. It has been our experience that in streptococcus endocarditis, no difficulty is found in demonstrating streptococci in and on the vegetation. In the present case, we were unable to demonstrate streptococci in the lesion, but were able to find large numbers of Gram negative diplococci in the cellular elements of the vegetation.

The streptococcus and colon bacillus were probably both terminal or post-mortem invaders. Neither of these organisms was found in any of the blood cultures taken. The eighteen hours which elapsed between the death of the patient and the autopsy gave opportunity for extensive multiplication of the colon bacillus in the blood. Its colonies occurred in large numbers in all the cultures, excepting the one from the vegetation.

The absence of meningococci from all the cultures taken at autopsy may be explained in several ways. The low vitality of the meningococcus, and the fact that it is usually intracellular make it a difficult organism to cultivate under the most favorable circumstances. On several occasions we have seen spinal fluids which contained meningococci in the leucocytes, but from which cultures were persistently sterile. Moreover, Flexner found that in the case of guinea-pigs killed by intraperitoneal injections of

meningococci, if the autopsies were delayed until partial decomposition of the body had set in, or if the dead pigs had been kept for many hours in the refrigerator, the chances of successful cultivation of the meningococcus were greatly reduced. He explains this in the first instance as probably due to the combined action of inflammatory exudate and the products of decomposition; in the second instance, to the low temperature. The fact that, in our case, the cadaver had been in the mortuary sixteen hours may have been responsible for the negative results obtained.

The second premise may, therefore, be accepted as proved, namely, that the vegetations were produced by the meningococcus.

A CASE OF MULTILOCULAR CILIATED CYST OF THE THORAX.

J. G. HOPKINS, M.D.

The specimen presented was found at the autopsy on the body of a female infant, four days old, dying of bronchopneumonia. On removing the lungs a small tongue-like mass was seen to project into the left pleural cavity from the angle formed by the diaphragm with the posterior thoracic wall and the mediastinum. The mass measured 2 x 1.5 x 1 cm., and was about the color and consistency of a spleen; but on section was found to be rather spongy.

Microscopically the growth was composed of branching acini lined by high columnar ciliated epithelium. In places the epithelium was desquamated in large sheets. The acini contained some coagulated albumin and a few large round desquamated cells. The interstitial connective tissue was very delicate and contained many large sinuses with very thin walls.

The chief point of interest in the case was the origin of this growth. Ciliated cysts of the esophagus have been described,

but they have all been unilocular or composed of a few chambers, and have been closely bound to the esophagus. They occur from the level of the thyroid down to the cardia; and many of them have shown smooth muscle and cartilage in their walls. Some unilocular ciliated cysts have also been found in the anterior mediastinum, on the surface of the liver, and in the suprarenals. None of these growths bore a very close resemblance to the one here described. The sections of this tumor strikingly resembled the epididymis, and the irregular arrangement of the acini suggested a rete. In mammalian embryos before the closure of the pleuro-peritoneal membrane the upper pole of the Wolffian body lies very close to the lung, and the Wolffian body begins to regress before this opening is closed. It would seem possible that some of the tubules of the cephalad portion might persist above the diaphragm. The fact that the blood supply of this growth came directly from the aorta by a lateral branch also suggested that it belonged to the urogenital system.

It was possible that sections from other portions of the tumor might throw more light on this question.

Discussion:

Dr. W. G. MacCallum agreed with Dr. Hopkins that the most plausible explanation of the origin of this tumor was that it was an inclusion of some portion of the Wolffian body, which, as is well known, undergoes extensive retrogression later.

A CASE OF CHORIOEPITHELIOMA OF THE BROAD LIGAMENT.

E. MOSCHCOWITZ, M.D.

Dr. E. Moschcowitz demonstrated a case of primary chorioepithelioma of the broad ligament. The patient was a woman, forty-six years old, who had had ten children, the youngest be-

ing seven years of age. One year before she had noticed that her abdomen was growing larger; and this enlargement was associated with other manifestations of pregnancy, nausea, enlargement of breasts, etc. The swelling of the abdomen continued for about six or seven months, at the end of which period she was curetted at Montreal, for a reason not ascertainable. The nature of the curettings also could not be determined. The patient was well for two or three months after this, when she began to develop some pain in the left side. On July 1, 1910, she was admitted to Beth Israel Hospital, and on vaginal examination a small mass was found to the left of the uterus anteriorly. There had been absence of menstruation for a month or two before admission, with occasional spotting, and a diagnosis of ectopic gestation was made. An operation was performed by Dr. Ladinski on July 3.

In the left broad ligament there was found a mass about the size of an orange, subtending the Fallopian tube, and having absolutely no connection with the ovary. The left border of the uterus formed the wall on the inner surface of the mass and was involved in the tumor growth. The uterine wall showed absolutely no infiltration. The two layers of the broad ligament formed the anterior and posterior walls of the tumor. Above, the Fallopian tube passed over the mass; below, the growth was in contact with the floor of the pelvis. The ovary was normal in size and position.

On section the tumor was firm, slightly softer in the center than at the periphery. The uterine border was irregular in outline and somewhat honeycombed in appearance. Both layers of the broad ligament were slightly thickened. The tube and ovary were not involved, and there was no loss of continuity anywhere. The uterus was normal in size, shape, and consistency; the uterine cavity was not enlarged, and had been freshly curetted.

The patient returned to the hospital about a month later, with symptoms of generalized malignant tumors of both lungs, and died within two or three weeks.

At autopsy, both lungs were found to be filled with multiple

tumors of enormous size. The entire lung was adherent. The
rest of the body was entirely free from metastatic deposits, with
the exception of the left kidney in which there was a small
growth, the size of a penny, near the pelvis. At the site of the
stump of the uterus a small mass, about the size of a marble, was
found. The nodule on the floor of the pelvis showed very beau-
tifully intravascular extensions of the chorioepithelioma.

Microscopical examination showed chorioepithelioma of the
typical type of Marchand. The curettings showed no mole nor
any evidence of chorioepithelioma. The picture was that of the
"interval" mucosa of Hitschmann and Adler.

Dr. Moschcowitz advanced three possible theories as to the
origin of the tumor:

1. That the supposed pregnancy was a hydatid mole, and
that the growth in the broad ligament was metastatic.

2. That there was a true pregnancy, and that the chorio-
epithelioma arose in a chorionic villus that had been projected
into the broad ligament.

3. That the tumor arose from a teratoma. Sections taken
from various parts showed absolutely no evidence of teratoma.
Dr. Moschcowitz was inclined to believe that the first surmise
was probably correct.

There was no connection with the tube or ovary. A pri-
mary chorioepithelioma of the broad ligament has not been re-
corded heretofore.

Discussion:

Dr. W. G. MacCallum expressed his interest in the case,
inasmuch as he had recently seen two similar ones. The first
was in a woman who had been operated on more than a year
before, both tubes and ovaries being extirpated. The condition
of these organs was not determined. The woman died with
symptoms of apoplexy, and at autopsy there was found an apo-
plectic form of hemorrhage in the cerebral hemisphere, sections
of the margins of which showed typical chorioepithelioma tissue.
There were similar hemorrhagic areas in the mesentery and

spleen, but the uterus showed no changes whatever. The second
case was one of well characterized chorioepithelioma developing
in the testicle. It would seem that these tumors must be looked
upon as a kind of teratoma developing from chorionic structures
which might or might not be connected with pregnancy.

A CASE OF INFECTION BY MUSCA STABULANS.

E. MOSCHCOWITZ, M.D.

The specimens of larvæ were found in the stools of a child,
six years of age, who was admitted to Beth Israel Hospital with
symptoms of an intense enterocolitis, with bloody stools, diar-
rhea, fever, and prostration. The fever was irregular, varying
between 101 and 103.5°.

On the ninth day of the illness, the larvæ were found in the
stools. These persisted for two or three days and then disap-
peared. The symptoms of enterocolitis, however, persisted, and
after a protracted convalescence the child was discharged from
the hospital at the end of three months.

Dr. C. W. Stiles, to whom some of the larvæ were sent for
identification, reported them as belonging to the Stabu fly. These
flies feed by preference on decaying fruits; and the child, who
lived in the most unhygienic surroundings, undoubtedly became
infected in this manner.

Infections of the intestinal tract by flies are not uncommon.
Of the more common species which have been found in human
beings, mention may be made of the ordinary fly (*Musca domes-
tica*), the "flesh" flies (*Sarcogaphidæ*), the "flower" fly (*Antho-
myia*), and the house fly (*Eristilax*). The symptoms of the in-
fection are those of an enterocolitis. There are a number of re-
ported cases of chronic infection, in which larvæ of flies appeared
at intervals in the stools, covering a course of one or two years,

Recovery is the rule. In fact, as far as Dr. Moschcowitz had been able to determine, the only fatal case on record was that of Schlesinger and Weichselbaum (*Wiener klin. Wchnschr.*, 1902). In this case a number of irregular ulcers were found throughout the colon.

A CASE OF INFECTION OF THE STOMACH OF THE HORSE WITH GASTROPHILUS EQUI (BOT-FLY).

E. MOSCHCOWITZ, M.D.

Dr. Moschcowitz showed a portion of the stomach of a horse. Numerous larvæ of *Gastrophilus equi* were found closely attached by their cephalic extremity to the mucosa. The vast majority of the larvæ were arranged in a line, just beyond a portion of the stomach in which the mucosa had been completely denuded, showing progressive destruction by the larvæ. The attachment of the larvæ to the stomach was close, and at the site of the attachment there was a round hole surrounding a slightly elevated crater-like projection.

Formidable as the lesion appeared, veterinarians are fairly well agreed that the infection is comparatively harmless. When the larvæ finally mature and are passed by the horse, regeneration of the mucosa takes place. In a few instances, perforation and peritonitis have been reported.

Infection occurs as follows: The bot-fly deposits its egg on the hairs of the horse, preferring the anterior aspects of the body. At the end of four or five days the larvæ break through the operculum and burrow into the skin. This burrowing causes itching, which the horse tries to relieve by rubbing the affected part with the tongue. In this way, the larvæ are swallowed. The larvæ mature in about ten months, usually between the months of May and August. They then pass from the rectum and mature as adult flies in about twenty days.

A CASE OF IMPACTED EGGS IN THE OVIDUCT OF A HEN;
A CASE OF TERATOMA OF THE SACRUM IN A HEN.

E. MOSCHCOWITZ, M.D.

During life the posterior portion of the hen was enlarged to the size of a child's head, rendering locomotion difficult. At autopsy the oviduct was filled with a very hard mass, made up of impacted eggs, which were closely compressed and appeared "hard-boiled." The shells were irregular in outline and were very soft. No stricture of the vagina was present.

The lesion was not uncommon in hens, and was usually found in old hens in whom there was a deficiency of lime in the shells of the eggs.

The specimen of teratoma consisted of a pair of short legs and the pelvis attached to the sacrum.

Discussion:

Dr. W. G. MacCallum said, with regard to the last specimen, that it was not to be regarded as a complete double monster, but rather as a rudimentary inclusion—a parasitic monster analogous to those in human beings in which a portion of an individual was found projecting from the sternum, palate, or elsewhere.

STUDIES ON THE EFFECT OF LECITHIN UPON THE FERMENTATION OF SUGAR BY BACTERIA.

ALBERT A. EPSTEIN, M.D., AND H. OLSAN, M.D.

This work was undertaken with a view to studying the effects of lecithin upon the process of sugar fermentation in vitro. Many functions have been ascribed to lecithin, and considerable discussion has arisen of late concerning its role in metabolism.

It has been assumed by a number of investigators that lecithin exerts an inhibitory action upon the oxidative processes in the animal body.

Diabetes has been claimed in some cases to be due to the inhibitory action of lecithin on the oxidation of sugar. This hypothesis has been chiefly upheld by Luethje, who found that the sugar output in diabetics was usually increased by the administration of egg yolk, a substance rich in lecithin. Bing, as is known, suggested that lecithin and dextrose combined in the blood, forming a substance called jecorin.

Some have even asserted that the alleged decrease in the intrinsic or fundamental metabolism, and the decrease in the oxygen consumption occurring in adiposis, are attributable to the presence of a larger amount of lecithin in the body fluids than that normally present. For example, Kempner and Schepilewsky found that white mice invariably increased in weight after receiving injections of lecithin.

Acting upon this belief, Russian and French investigators have suggested the use of lecithin therapeutically in cases of emaciation and wasting diseases. In support of their claims, the authors quote a number of experiments made upon animals, the results of which do not appear as convincing as the authors believe them to be.

Lately Yoshimoto made a number of animal experiments with lecithin, and instead of finding a diminished output of nitrogen in the urine, he found it to be increased—the increase being the exact equivalent of the nitrogen present in the lecithin administered to the animals. This investigator, therefore, came to the conclusion that lecithin does not exert an inhibitory action on metabolism.

The attempt to ascertain any such function of lecithin in vivo is naturally associated with many difficulties. Even were we to find a diminution in the nitrogen output after feeding lecithin to animals, the conclusion that lecithin produced this result by virtue of its action upon nitrogenous metabolism would not be justifiable. Such a result might be due to an indirect action; for

example, we could readily conceive of an increased mobilization of fats produced by lecithin; or possibly even an increased oxidation of sugars, the result of which would be a sparing of proteid material, leading consequently to a diminished output of nitrogen in the urine. This effect would manifestly be, not the result of inhibitory action of lecithin upon nitrogenous metabolism, but the indirect result of an increased combustion of fats and sugars.

The difficulties which arise in the study of a problem of this character in vivo are chiefly due to the fact that it is almost impossible to dissociate a single function or chemical process from every other in the body.

It seemed, therefore, desirable to approach the subject in a somewhat simpler way. Vallet and Rimbaud, as well as Renshaw and Atkins, have recently attempted to solve the problem of the role of lecithin in biological processes, by studying its effect upon the growth of bacteria. Their results show that lecithin does not materially influence the growth of bacteria. However, the method pursued by the above investigators, when taken in conjunction with the object sought after, is not free from criticism. Cellular growth and cellular function should not be confused; the one need not be an index of the activity of the other. The protoplasm of many cell and tissue-forms is endowed with some of the functions present in the living cells. This is true of many enzyme or ferment-bearing cells. The extract of the yeast cell, for example, can ferment sugar as the living cell itself.

Here we have a function that is resident in the cell material and is active even in the absence of cell life. A number of experiments have been made by Kuettner, and also by O. Schwarz, with lecithin and the different digestive ferments. Schwartz, for example, ascribes the inhibitory action of blood serum upon trypsin, to lipoids, presumably lecithin.

We have, therefore, deemed it necessary to take up the study of lecithin in connection with the fermentation of sugars by bacteria. In so doing we deal with a single comparatively simple process in which oxidation plays the chief role. The character

of the agents used in the tests to produce the fermentation is also relatively simple.

For our purposes we used three types of bacteria; namely, *Bacillus coli communis, Bacillus mucosus capsulatus,* and *Bacillus acidi lactici.* Each of these organisms ferments certain sugars. Our measure of bacterial activity, therefore, was the production of gas and acid.

The amount of lecithin employed in our media at no time exceeded 0.4 per cent. This, of course, is an amount of the substance in excess of that found in biological fluids. If, therefore, lecithin could modify oxidative processes in respect to sugar fermentation, then it would manifest itself by an increase or decrease in the production of gas or acid, or both. We tested the fermentative action of the above bacteria on twelve different types of sugars. This was done to ascertain whether or not the chemical constitution of sugar played any role in the rate and character of its decomposition by bacteria.

The list of sugars includes the alcohol, aldehyde, and ketone type of the different saccharides (mono- di- and polysaccharide.) A hexavalent alcohol and an aldehyde pentose are also represented in the series.

A 1 per cent. solution of each sugar in nutrient bouillon (neutral to phenolphthalein) was used. The media were distributed into fermentation and straight test tubes, 10 c.c. of each medium being used as the unit. To one set of tubes, a 4 per cent. emulsion of lecithin was added, allowing 1 c.c. for each tube. To the other set, sterile salt solution was added in like amount.

Both sets of tubes were inoculated with a loopful of an emulsion of each bacterium and incubated at 37.5° C. All the tests were made in duplicate. A parallel series of uninoculated tubes were incubated and used as controls.

The amount of gas produced in the fermentation tubes was recorded in cubic centimeters at the end of twenty-four and forty-eight hours' incubation. The following table shows the results obtained in tests on gas production:

TABLE 1.—SHOWING GAS PRODUCTION IN CUBIC CENTIMETERS.

	MONOSACCHARIDES			DISACCHARIDES			TRI-SACCHARIDE	POLY-SACCHARIDES		TRIVALENT ALCOHOL	HEXAVALENT ALCOHOL	ALDEHYDE PENTOSE
	Dextrose	Galactose	Levulose	Maltose	Lactose	Saccharose	Raffinose	Inulin	Dextrin	Glycerine	Mannit	Arabinose
Bacillus coli communis												
Plain medium { 24 hrs.	1.0	1.0	1.0	2.0	2.0	0.5	2.0	0	0	0	3.0	1.0
{ 48 hrs.	1.0	2.0	2.0	3.0	2.0	1.0	2.0	0	0	0	4.0	1.0
Plain medium { 24 hrs.	1.0	2.0	1.0	2.0	3.0	1.0	0.5	0	0	0	3.0	1.0
with lecithin { 48 hrs.	2.0	3.0	2.0	3.0	4.0	2.0	0.5	0	0	0	4.0	1.0
Bacillus mucosus capsulatus												
Plain medium { 24 hrs.	2.0	2.0	2.0	2.0	2.0	0	0	0	0	0	3.0	2.0
{ 48 hrs.	2.5	2.0	2.0	2.5	2.0	0	0	0	0	0	3.0	3.0
Plain medium { 24 hrs.	1.0	2.0	2.0	2.0	1.0	0	0	0	0	0	3.0	1.0
with lecithin { 48 hrs.	2.0	3.0	3.0	2.5	1.0	0	0	0	0	0	4.0	2.0
Bacillus acidi lactici												
Plain medium { 24 hrs.	2.0	3.0	4.0	2.0	2.0	2.0	3.0	0	0	0	3.0	1.0
{ 48 hrs.	2.0	5.0	4.0	2.0	5.0	4.0	3.5	0	0	0	4.0	2.5
Plain medium { 24 hrs.	1.0	2.0	2.0	2.0	2.0	4.0	1.0	0	0	0	1.0	1.5
with lecithin { 48 hrs.	3.0	3.0	3.0	3.0	4.0	5.0	2.5	0	0	0	4.0	3.5

SUMMARY.

Bacillus coli communis.

Increased gas.	*Decreased gas.*	*No effect.*
Dextrose	Raffinose	Levulose
Galactose		Maltose
Lactose		Inulin
Saccharose		Dextrin
		Glycerine
		Mannit
		Arabinose

Bacillus mucosus capsulatus.

Increased gas.	*Decreased gas.*	*No effect.*
Galactose	Dextrose	Maltose
Levulose	Lactose	Saccharose
Mannit	Arabinose	Raffinose
		Inulin
		Dextrin
		Glycerine

Bacillus acidi lactici.

Increased gas.	*Decreased gas.*	*No effect.*
Maltose	Galactose	Dextrose
Saccharose	Lactose	Inulin
Dextrin	Levulose	Glycerine
Arabinose	Raffinose	

In the above table we note that with *Bacillus coli communis,* lecithin favors an increase in gas formation in the monosaccharides dextrose and galactose, and the disaccharide lactose; while it inhibits gas formation in the trisaccharide raffinose. The remaining sugars are unaffected.

Lecithin aids gas production by *Bacillus mucosus capsulatus* in the monosaccharides galactose and levulose, while it arrests gas production with dextrose. Lactose and arabinose are influenced in like manner.

With *Bacillus acidi lactici* lecithin also aids the formation of gas in the disaccharides maltose and saccharose, while it checks gas fermentation in all the monosaccharides, excepting dextrose, in the disaccharide lactose, and in raffinose and in mannit. The remaining media are unaffected.

TABLE 2 (a).—SHOWING ACID PRODUCTION IN THE DIFFERENT SUGAR MEDIA—IN C. C. OF N/10 NaOH

| | Monosaccharides | | | Disaccharides | | | Tri-saccharide | Poly-saccharide | | Trivalent Alcohol | Hexavalent Alcohol | Aldehyde Pentose |
	Dextrose	Galactose	Levulose	Maltose	Lactose	Saccharose	Raffinose	Inulin	Dextrin	Glycerine	Mannit	Arabinose
Plain medium—control	0.2	0.35	0.7	0.35	0.6	0	0	0	0.15	0	0	0.65
Plain medium Bac. coli com.	7.1	4.6	5.1	4.4	5.2	0	1.05	0.4	0.12	0	4.2	3.60
Net acid produced	6.9	4.25	4.4	4.05	4.6		1.05	0.4	0.03	0	4.2	2.95
Plain med. Bac. muc. caps.	0.45	0.35	4.3	0.5	0.9	0	0	0	0.02	0	0	0.45
Net acid produced	0.25	0	3.6	0.15	0.3	0	0	0	0.05	0	0	0.20
Plain med. Bac. acidi lact.	4.0	5.5	4.8	7.6	4.9	4.8	4.7	2.85	4.5	0	6.15	7.85
Net acid produced	3.8	5.15	4.1	7.25	4.3	4.8	4.7	2.85	4.35	0	6.15	7.20

TABLE 2 (b).—SHOWING ACID PRODUCTION ON THE SUGAR MEDIA IN THE PRESENCE OF 0.4% LECITHIN.

| | Monosaccharides | | | Disaccharides | | | Tri-saccharide | Poly-saccharide | | Trivalent Alcohol | Hexavalent Alcohol | Aldehyde Pentose |
	Dextrose	Galactose	Levulose	Maltose	Lactose	Saccharose	Raffinose	Inulin	Dextrin	Glycerine	Mannit	Arabinose
Lecithin medium—control	1.75	1.6	1.45	1.4	1.9	0.3	0	0.5	1.35	0.3	0.95	2.0
Culture Bac. coli communis	4.5	5.8	7.85	—	6.3	1.2	0	1.85	1.5	0.1	7.55	5.1
Net acid produced	2.75	4.2	5.4	—	4.4	0.9	0	1.35	0.15	— 0.2	6.65	3.1
Cult. Bac. muc. caps	6.1	2.15	8.35	—	2.6	0.5	0	0.35	0.95	0	0.9	4.1
Net acid produced	4.35	5.5	6.9	—	0.7	— 0.2	0	—0.15	— 0.4	— 0.3	— 0.05	3.9
Cult. Bac. acidi lact.	9.1	9.4	7.8	12.5	10.5	12.0	9.8	5.3	6.70	—	7.4	9.5
Net acid produced	7.35	7.80	6.35	11.1	8.7	11.7	9.8	4.8	5.35	—	6.45	7.5

As the above tables indicate, the results of acid production are more uniform than those obtained with gas production. *Bacillus coli communis* causes an increased acid production in the presence of lecithin with all the sugars excepting dextrose and raffinose. With the latter two sugars this bacillus produces less acid in the presence of lecithin than otherwise.

Bacillus mucosus capsulatus produces more acid in the presence of lecithin than otherwise, with all the sugars excepting glycerine and raffinose; upon the latter lecithin has no effect. *Bacillus acidi lactici* in the presence of lecithin produces more acid in all the sugar media.

It is significant that in all the acid tests lecithin has a distinct tendency to increase rather than to decrease the acid production; and if we take acid production as an index of oxidative processes, then we must conclude that lecithin aids oxidation of the sugars.

It is necessary to call attention to the fact that in all our tests lecithin is presumably present in a free state; and although we have reasons to believe from the work done by one of us (E.) in another connection, that lecithin enters into combination with peptone bodies, such as are present in our culture media, we must for the present infer that the lecithin present is in a free state; and the conclusions to be drawn must apply to the action of lecithin present in this state.

To summarize briefly, our conclusions, therefore, are: (1) Free lecithin may modify the bacterial fermentation of different sugars; and hence oxidative processes. (2) The action of lecithin increases the fermentation of some sugars and lessens that of others. There is apparently no definite relationship between the action of lecithin upon the sugars, and their chemical composition.

To sum up: the tendency of lecithin is to increase rather than to decrease fermentation, and consequently oxidation.

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CASE OF RUPTURE OF THE HEART DUE TO CORONARY HEMORRHAGE.*

J. G. HOPKINS, M.D.

This specimen was obtained at autopsy on the body of a woman of fifty years, a designer by occupation. The patient had always been well, except for the diseases of childhood, up to four days before admission to the hospital, when she had a sudden sensation of suffocation while at work and had to be taken home. This attack was followed by rather severe constant pain in the precordia which increased on deep breathing. She had no other symptoms. On examination the apex beat was not made out. The heart dulness was apparently increased; the sounds were distant but normal; no murmurs were heard. The pulse was regular and of good force. After rest in bed the pain disappeared, and on the third day the patient was allowed to sit up, with the expectation of discharge in a few days. While being wheeled to her bed after defecation she became deeply cyanotic, fell forward in her chair, and apparently died instantly.

At autopsy the pericardium contained coagulated blood which formed a thick layer about the anterior, posterior, and right surfaces of the ventricles and extended up about the aorta and pulmonary artery. The clot was thickest at the apex posteriorly, where it measured 2.5 cm. In the apex of the ventricle was a blood clot about 2 cm. in diameter, and in the anterior wall near the septum was a cleft filled with blood clot, continuous with that in the ventricle. This cleft extended downward and to the left, following the course of the muscle fibers. At the left border of the heart it reached the subpericardial fat and extended through the fat communicating with the pericardium apparently at the apex posteriorly, though the precise point of communication was not made out. There was also hemorrhage in the fat below and about the apex of the right ventricle. The ventricles were in complete systole, as is usual in these cases. The left auricle was considerably dilated, and the right con-

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*From the Pathological Department of St. Luke's Hospital, New York.

tracted or compressed. The valve leaflets were thickened; but on inspection through windows cut in the wall no stenosis or insufficiency could be made out. The coronaries showed extensive sclerosis, and the descending branch of the left coronary was much thickened and diffusely calcareous. The external diameter of this vessel was about 4 mm., but its lumen was very small. About 4 cm. from its origin the lumen was practically occluded by the thickening, and was filled with a thrombus; but could be traced on section 1 cm. or more below this point. The anterior wall of the left ventricle in the region supplied by this artery was pale yellow and appeared necrotic. Microscopically this area showed complete hyaline necrosis of the muscle cells. The thrombus, which to the naked eye appeared to lie in the ventricle, was found to be covered by a layer of endothelium. The blood clot in the ruptured wall was surrounded by large numbers of polynuclear leucocytes. Whereas anteriorly the muscle cells to either side of the hemorrhage were necrotic, posteriorly, near the point of communication with the pericardium, they were fairly well preserved. The aorta showed extensive arteriosclerosis with calcification.

There was marked interstitial nephritis. The liver showed chronic passive congestion with extensive deposits of fat and blood pigment. The lungs were emphysematous, markedly congested, and edematous at the bases, and showed some scars of old tuberculosis.

The fact that the blood clot lay beneath the endocardium made it seem probable that this was a rupture due to hemorrhage from the coronary vessels, which extended internally beneath the endocardium and externally into the pericardial sac. The endocardium was intact apparently, and there was no escape of ventricular blood. From the amount of reaction about the clot it was probable that the first hemorrhage into the wall occurred when the patient had her first attack of pain; the terminal event was probably the rupture of this hemorrhage into the pericardium.

The experiments of Cohnheim on increase of fluid in the

pericardium showed that a sudden increase of 150 to 200 c.c.
was sufficient to cause death, whereas a much larger amount of
fluid might accumulate gradually in the pericardium without a
fatal result. The effect depends upon the tension of the fluid
rather than upon its amount. As the pericardial pressure ap-
proaches the pressure in the right auricle it interferes with the
entry of blood into the heart from the systemic veins. The
pressure in the left auricle is considerably greater than in the
right, and consequently the entry of blood from the lungs is not
interfered with until the pericardial pressure is increased con-
siderably above the point necessary to compress the right auricle.
In the dog a pressure of 60 mm. of mercury was found to be
sufficient to block the entry of blood from the systemic veins,
causing a rise in venous pressure and a fall in arterial pressure.

In the case reported, the collapsed condition of the right
auricle and the dilatation of the left auricle bear evidence that
death was due to increased pericardial pressure.

Rupture of the heart is among the rarer causes of sudden
death and has aroused much interest since the first case described
by Harvey. Morgagni described a number of cases from his
own experience, but the lesion appears to be much less frequent
in recent times. Elleaume collected sixty-one cases, thirty-seven
of which were in men and twenty-four in women. The rupture
is usually very minute, as in this case, and usually larger exter-
nally than internally. The cleft, as a rule, follows the course of
muscle fibers; occasionally there is a long tear—in one case from
the base to the apex; and from three to five multiple tears have
been reported. Forty-three of fifty-five cases involved the left
ventricle, and the usual point was in the anterior wall near the
apex. The rupture may follow embolic or sclerotic occlusion of
the coronary artery with subsequent softening of the wall. Ab-
scesses in the myocardium, gummata, and tumors have also lead
to rupture. Ten of Elleaume's cases were due to rupture of an
aneurism of the heart, which is a relatively frequent cause.

Quain suggested that diffuse fatty change might lead to
rupture, but this seems unlikely as it lessens the force of the
heart action and would rather tend to prevent rupture.

Rupture of the heart occurs in old age and usually after severe exertion. It sometimes occurs without any apparent occasion, and even while the patient is asleep. In other cases it may follow psychical excitement, as in the case of Philip the Second of Spain who died of rupture of the heart when told of the defeat of his armies.

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CASE OF ANEURISM OF THE AORTA WITH RUPTURE INTO THE TRACHEA.*

J. G. HOPKINS, M.D.

The specimen was obtained at autopsy on the body of a German machinist, 59 years of age, who died suddenly shortly after admission to St. Luke's Hospital. He gave a doubtful syphilitic history. He had had no symptoms referable to the aneurism up to one month before death, when he developed a cough with muco-purulent expectoration, which was increased on lying down. About the same time he began to suffer from dyspnea on exertion. The night before admission to the hospital he had a slight hemoptysis.

On admission he was given a bath, and was sitting beside his bed while it was being made up, when he had a severe paroxysm of coughing, brought up several ounces of bright frothy blood, became deeply cyanotic, and died.

At autopsy there was found in the thorax a huge aneurism involving the entire arch and passing without definite boundary

*From the Pathological Department of St. Luke's Hospital, New York.

into the sclerotic descending aorta. The heart was slightly enlarged and was displaced downward and to the left. When the body was opened the aneurism was collapsed. After distending the sac with very little pressure the ascending portion of the aorta measured 8 cm. in diameter, the transvere portion 9 cm. in its greatest diameter, and the descending portion 4.5 cm. on an average. The inner surface was irregular and covered with raised wheals, and presented numerous hard plaques with beginning calcification. In the posterior wall of the aorta there was a small opening about 2 cm. in diameter which led into a small, comparatively thin wall sac which was adherent to the anterior surface of the trachea. The sac contained a few small thrombi, and beneath one of these, which lay on the posterior wall, there was a small sinus communicating with the trachea just above the bifurcation.

The bronchi were filled with blood and the lungs were congested and extremely edematous.

Rupture of an aneurism into the trachea is one of the most common forms of termination according to Osler, though it is not mentioned in Lebert's series of forty-two cases of rupture. It is not necessarily fatal, and numerous cases of temporary recovery have been reported since that of Zehetmayer in 1845. Premonitory bleedings such as occurred in this case are very common. The large callous cylindrical aneurism probably existed long before the onset of the patient's symptoms. It seems likely that the first symptoms were brought on by the growth of the small saccular aneurism from a thickened part of the posterior wall in the older sac. This is the situation where aneurisms produce symptoms early, the first sign sometimes being fatal rupture into the air passages.

Discussion:

Dr. WOOD thought it remarkable that a person could so long survive serious injury to the heart with concurrent hemopericardium. Such severe lesions would usually be thought of as lead-

ing to instant death. In a case which he had himself observed, however, the patient, an Italian, had been shot through the sternum, the bullet entering the auricle. After the shooting the man ran two or three blocks down the street to his home and went to bed, where he stayed for two or three days without complaining of anything but slight headache. His family did not know there was anything wrong with him until he died suddenly. At autopsy it was found that the auricle was open and the pericardium filled with blood.

DR. LOUIS F. BISHOP said that his experience in the hospital with this class of cases was that they had lived much longer than one would think possible when a large amount of blood was found in the pericardial sac. He congratulated the presenter of the specimen upon the beautiful way in which it was prepared, such specimens usually being spoiled by carelessness when they were first discovered.

DR. JAMES EWING remarked that an obscure point in these cases was the manner of death. The history of the case under discussion pointed rather distinctly to a sudden onset of symptoms which ought to be accompanied, it seemed to him, by the presence of some signs of recent hemorrhage. He had understood that Dr. Hopkins had not been able to find an area where recent extravasation of blood had occurred. Dr. Ewing had the impression that this clot was all rather old, and that no recent hemorrhage had been found. It seemed to him that in many of these cases it was extremely difficult to determine the cause of death, and a recent experience which he had had seemed to be worth reporting in this connection. A man had suffered a penetrating wound of the chest wall from a long needle about the size of a hat pin, against which he fell, driving the needle through the chest wall and apparently through the heart. He was carried to the hospital, and the house surgeon found nothing but a small puncture over the region of the left ventricle. The needle had been broken off, and the end was just beneath the skin. The patient suffered very severe pain, dyspnea, and shock, remaining in that state for six hours, when he died. The autopsy

showed a needle penetrating the wall of the left ventricle, but not entering the cavity. There were six ounces of blood in the pericardial cavity. The heart itself was absolutely sound, except for the trauma. The coronary vessels were sound. The only thing that could account for death was the loss of blood, and apparently the nervous shock arising from the wound.

A CASE OF SCHISTOSOMUM JAPONICUM.

RUSSELL L. CECIL, M.D.

The patient was a Japanese, twenty-eight years of age, who was admitted to the Second Medical Division of the Presbyterian Hospital on November 21, 1910. Five weeks before he had been in Bellevue Hospital for an attack of "fever." The family and previous personal history was otherwise negative; there was no history of gastric disturbances. On the evening preceding admission, after an ordinary dinner, he vomited food and a considerable quantity of bright red blood. This vomiting was repeated once or twice during the night. On admission, about eleven a. m., he was very pale, but free from pain or distress of any kind.

Physical examination showed a spleen reaching to the umbilicus; no other item of importance. During the day the patient was comfortable, but the vomiting of blood recurred during the night, and was repeated a number of times, a total of about forty-eight ounces being raised. He died the following morning about twelve o'clock.

The autopsy was performed on November 23, twenty-five hours post-mortem. The body was that of a young Japanese, and measured 150 cm. in length. Post-mortem rigidity was present; livor mortis in dependent parts. Pupils were equal and moderately dilated. On opening the abdomen, the peritoneal surfaces were smooth and glistening. There were a few adhe-

sions about the appendix, and the neighboring fat contained considerable dense fibrous tissue.

The heart weighed 280 grams. The pericardial sac was normal. The epicardium was smooth and glistening. The tricuspid and pulmonary valves were normal. The aortic leaflets were slightly thickened. There were a few plaques of atheroma at the base of the aorta. The left ventricular wall measured 13 to 15 mm. in thickness. The myocardium was dark brownish in color. The coronary arteries were normal.

The right lung weighed 330 grams: it lay free in the pleural cavity: and its surfaces were translucent and glistening. The tissues were everywhere crepitant. The cut surface was pale. The structures at the hilum were normal. The left lung was collapsed and everywhere adherent to the thoracic wall and the diaphragm. The pleural covering of the lung was considerably thickened, especially along the posterior border, where it formed a thick white dense membrane. The left lung weighed 320 grams with the diaphragm attached. The tissue was resilient and contained very little air. The cut surface was dark and hemorrhagic. The structures at the hilum were normal.

The spleen was greatly enlarged. It weighed 900 grams, and measured 22 x 15 x 8 cm. The surface was pinkish red, and smooth and glistening. The organ had a firm, leathery consistence, and the cut surface was pinkish red and oozed very little pulp. The Malpighian bodies and trabeculæ were prominent. The splenic artery and vein were free from thrombosis.

The liver weighed 1400 grams. It was somewhat smaller than normal, and very firm in consistence. The surface had a pale, grayish brown color, and was coarsely granular, the lobules being separated by irregular fissures of various depths. On the inferior surface of the liver the fissures were deeper than elsewhere and divided the surface into a large number of nodules varying from 0.1 to 2 cm. in diameter. The cut surface of the liver was pale brown and opaque. The normal lobulation had been destroyed, and replaced by lobules of various sizes separated by translucent anastomosing bands.

The gall-bladder contained dark brown viscid bile. The bile ducts were patent. There was no thrombosis of the portal vessels.

The pancreas was pale and firm. On section the lobules were easily separated; a few islands were visible. The pancreatic duct was patent. The lymph. nodes surrounding the pancreas was enlarged.

The left kidney weighed 120 grams. The capsule stripped easily, exposing a smooth and pale surface. On section the cortical markings were distinctly seen. The pyramids were sharply defined. The right kidney weighed 110 grams. It was similar to the left in all respects. Pelvis and ureters were normal.

The suprarenal glands were normal.

The bladder was normal.

The rectum contained dark, black tarry material, evidently old blood. There were a few small dark irregularities in the mucosa which had the appearance of healed ulcers.

The mesenteric lymph nodes were not enlarged.

The aorta was elastic and there were a few plaques of atheroma.

The esophagus showed a few dilated and tortuous veins.

The stomach was moderately dilated and contained dark red fluid blood. The gastric mucosa was dark red, glistening, and mottled with small dark spots at many points. At no point, however, was there any break in the mucosa.

The duodenum contained dark reddish brown material.

The jejunum and ileum contained dark red coagulated blood. The mucosa of the small intestine was everywhere smooth and pale. The solitary follicles in the small gut were prominent. Surrounding the head of the cecum there was some dense fibrous tissue which, on section, presented the appearance of a healed focus of some kind. Just below the ileocecal valve there were several small dark red polypoid projections on the surface of the mucosa which had the appearance of polyps.

The large intestine was filled with black tarry material. The mucosa of the large intestine was, for the most part, smooth and glistening.

Microscopical Examination.

Spleen: Sections showed considerable increase in interstitial tissue. The new formed tissue was fairly dense and contained small spindle shaped nuclei. In the interstices of the connective tissue, red blood cells and leucocytes, chiefly of the lymphoid variety, occurred in considerable numbers. The walls of the blood vessels were much thickened, and there was considerable hyaline degeneration in the dense fibrous tissue around them. In many places the red blood cells showed signs of disintegration.

Liver: There was a well marked increase of connective tissue between the lobules and along the courses of the portal vessels. The new formed tissue was dense and infiltrated with considerable numbers of lymphoid cells. There was some regeneration of small bile ducts. At many points in the stroma there could be seen one or more ova lying in the interstices of the tissue; they were oval shaped and surrounded by a thin refractile capsule. Segmentation had occurred in some of the ova. A few of the ova had penetrated into the lobules. Smaller arteries throughout the stroma showed a marked thickening of the intimal coat. The parenchyma was normal.

Pancreas: There was no increase in the interstitial tissue. The islands were rather scarce.

Heart muscle: Normal.

Kidneys: Normal.

Suprarenal glands: Medulla showed post-mortem degeneration. The cortex was normal.

Lungs: The interalveolar septa were congested. Pleura was greatly thickened and hyaline.

Appendix: Normal.

Retroperitoneal lymph node: A small collection of ova, resembling those found in the liver, was found in one of the sinuses. Chyme centers were swollen.

Rectum: Section through one of the small scars showed the following: The mucosa was intact. In the submucosa there was a dense collection of ova similar to those described in the liver. They were separated from one another by connective tissue which showed little or no infiltration. Segmentation had occurred in some of the ova. Small groups of ova occurred here and there in the interstitial tissue of the muscularis. The subserosa also contained small masses of ova. Sections from the ileum and the cecum showed same condition.

Anatomical Diagnosis: Ova of *Schistosomum japonicum* in submucosa of intestine, liver, and retroperitoneal lymph glands. Chronic peritonitis. Splenomegaly. Interlobular sclerosis of liver. Hemorrhages into gastrointestinal tract. Chronic fibrous pleuritis. Atelectasis of left lung.

Schistosomum japonicum infections occur endemically in certain provinces in Japan. They are characterized by enlargement and cirrhosis of the liver, enlargement of the spleen, bloody

diarrhea, anemia, and cachexia. Ascites and edema occur in some cases.

As far back as 1888, Majima in Tokio found peculiar ova in the liver of a case of cirrhosis. These he described as the ova of an unknown parasite. It was not until 1904 that Katsurada discovered the parasite in two cats from the province of Yamanaski. These parasites were found in the portal veins and contained ova identical with those previously found in man.

Shortly after this, Fuginami observed several cases, some of them coming to autopsy. He found the ova in the liver, intestinal wall, and mesenteric glands, and also found one of the parasites in a branch of the portal vein.

Morphologically, *Schistosomum japonicum* closely resembles *Schistosomum hematobium*. The distinguishing characteristics of the japonicum are: (1) Its smaller dimensions, only 9 to 12 mm. in length; (2) the larger size of the acetabulum as compared to the oral sucker; (3) the ova, 70 to 75 microns in length, have a smooth capsule instead of one with a spine like that of the hematobium. The ova resemble somewhat those of the uncinaria.

The pathological anatomy of the disease corresponds closely with that found in the case I have reported. The intestinal lesions are chiefly in the large intestine. The wall of the colon is thickened, and there are adhesions about it. Its mucous membrane is swollen and hyperemic, and presents numerous small erosions and patches of necrosis.

The liver is enlarged and hard; its surface is nodular. The mesenteric and retroperitoneal glands are hypertrophied. The spleen is generally quite large and firm in consistence. The urinary bladder is not affected. This constitutes another point of distinction from *Schistosomum hematobium* infection, in which the bladder and genito-urinary tract are involved.

The case reported is evidently a healed case. There were no definite breaks in the intestinal mucosa. The Peyer's patches and solitary follicles were prominent, but there was no ulceration. Many of the ova in the liver showed degenerative changes.

The patient's death was due to hemorrhages following advanced cirrhosis of the liver, the cirrhosis, of course, being the sequel of the schistosomum infection.

Discussion:

Dr. R. M. Pearce said that Dr. A. J. Smith, of Philadelphia, has made a study of what was apparently the first case of this disease in the Caucasian race—an American child living in China. Although Dr. Pearce was not very well acquainted with the facts of the case, he thought it interesting in that so far as Dr. Smith knew no other case had ever been reported in the Caucasian race.